# Involvement in research and service improvement


SCIENCE FOR ALL

# Facilitator manual

# About this document

This document was created for Arthritis Australia by Jack Nunn, Director of 'Science for All'. It contains a facilitation plan and resources for running a learning event. All these resources are licensed under Creative Commons.

### About Science for All

'Science for All' is a not-for-profit organisation that supports everyone in the world to get involved in shaping the future of human knowledge. Learn more at scienceforall.world

### Aim of the learning session:

To enable and empower participants to understand how the public can become effectively involved in shaping the future of research, including reviewing research proposals and improving services.

## Outcomes

After attending, participants will be able to:

- Explain what public involvement in research is and why it is important
- Explain ways of involving people in research service improvement
- Explain what critical appraisal of research is and know how to use relevant resources
- Explain what health technology assessment is and why involvement is important

## Timings

This face to face training session will be designed to be flexible and run for total of 2 hours.

## Delivery

In order to achieve specific learning outcomes, this learning event will be delivered using a combination of:

- Pre-prepared learning resources
- Interactive activities (including opportunities to apply learning using simulated examples)
- Facilitated discussions

If Arthritis Australia wish to include people who cannot physically attend, then this training session can be designed to include people joining through telecommunications. The proposed platform for delivery is Zoom, which will allow people with a range of devices to join the discussion – including over the telephone. People using computers and smart phones can use the screen to read relevant resources, while people joining over the phone can have documents sent in advance electronically or via post if appropriate.

If people are joining online, a certain level of computer literacy will be assumed, for example, being able to open and navigate a PDF document and follow links within it.

## Contents

# Detailed Learning Plan

A detailed learning plan can be found on the next page.

| Session | Summary | Learning aims | Learning outcomes | Activity instructions | Resources | Time |
|---|---|---|---|---|---|---|
| Introductions | Introductions and expectations | To provide a general outline of course and to give participants chance to introduce themselves | Participants will be able to explain the purpose of the course and what they will learn | • Introduce self and explain format of the course.<br>• Invite people to introduce themselves via chat and state what they'd like to get out of the session<br>• Summarise back themes and check learning aims will be met | | **10** |
| What is involvement in research? | An exploration of the meanings of the word 'research' | • To help define what is meant by the word 'research'<br>• Focus participants on the whole research process, rather than just reviewing research proposals.<br>• To articulate what 'involvement' means | • Be able to explain the terms 'research'<br>• Be able to explain why we do research<br>• Be able to explain why we involve people | Assess group knowledge:<br>• Ask people what they understand by the terms 'research'<br>• Does anyone have an examples of it that they know?<br><br>Read out definition:<br>The National Health and Medical Research Council defines involvement as:<br>"research being carried out with or by consumers and community members rather than to, about or for them'<br><br>State that detailed explanations are in the resources that will be shared. Mention briefly that the word 'consumer' is used in Australia but that you will use 'public'.<br><br>• Now ask people **why** we do research and have health services (typical answers are 'improves lives', 'happier', 'better quality of life').<br><br>• Now ask people why you should **involve the public** in research.<br><br>• Tell the 'Why we involve the public' story from the 'Resource 2: Stories and facts about public involvement in research' or use any from your own experience. | Resource 1: Public Involvement in Clinical Trials<br><br>Resource 2: Stories and facts about public involvement in research<br><br>Resource 3<br>Resources 3.1 and 3.2<br>Resource 4<br>Resource 5<br><br>Resource 19 | **15** |

| Session | Summary | Learning aims | Learning outcomes | Activity instructions | Resources | Time |
|---|---|---|---|---|---|---|
| Research Methods and terminology | How research is conducted and the terminology used | To introduce some of the language and methods of research and how our perceptions may be affected by media coverage | • Be able to explain the different methods of research used and the language used to describe it<br>• Explain what critical appraisal is | Explain that there are a variety of research methods. Explain that the terminology is there to ensure everyone, both those doing the study as well as anyone enquiring about it, understands the process under which that particular research study is being undertaken (**3 minutes**).<br><br>Distribute the 'Types of research' resource and the 'Blank definitions of research' resource and ask each group to choose a spokesperson and then to match the title with the description (you may want to produce cards that people can place on the terms).<br><br>Leave the groups to work for about 5 minutes and give them a minute's warning before ending the session. Allow (**5 minutes**).<br><br>Highlight that there are arrows on the sheet (one pointing to the future, the other to the past) and explain that this is a hint as to the direction of time for the type of research it is next to.<br><br>Ask the groups to give their answers. Then use an example of each to ensure they understand the process named (use 'Definitions of research' resource for real life examples) **(5 min)** **Answers: Link to answers is here or found in the resources**<br><br>Refer to 'common terms' for vocabulary. | Activity 1: Match the definitions<br><br>Resource 20: Common terms | **15** |

<table>
<tr><th>Session</th><th>Summary</th><th>Learning aims</th><th>Learning outcomes</th><th>Activity instructions</th><th>Resources</th><th>Time</th></tr>
<tr>
<td>The research cycle and public involvement</td>
<td>How and where the public can be involved in research</td>
<td>To use the research cycle as a basic model for understanding the different stages of the research process and to explore the added value of public involvement</td>
<td>Participants will be able to explain:<ul><li>The various stages of the research cycle, including the stages of a clinical trial</li><li>The importance of involving the public at every stage and the ways people can get involved.</li><li>The different tasks people can be asked to do</li><li>The difference between ‘patient and carer’ involvement, ‘lay’ involvement and that the word ‘public’ encompasses them all, but sometimes needs articulating.</li></ul></td>
<td><ul><li>Ask participants to put the research cycle stages in order</li><li>Ask participants to put the phases of a clinical trial in the right order</li></ul>
<table>
<tr><th>Phase</th><th>Letter</th></tr>
<tr><td>Pre-Clinical</td><td>Z</td></tr>
<tr><td>0</td><td>Y</td></tr>
<tr><td>I</td><td>X</td></tr>
<tr><td>II</td><td>W</td></tr>
<tr><td>III</td><td>U</td></tr>
<tr><td>IV</td><td>T</td></tr>
</table>
Questions to discuss:
<ul><li>How could the public be involved in each of these stages?</li><li>Which stage might you want to consider specifically involving patients with relevant experience and why?</li><li>Phase Y talks about different types of research to evaluate research. What kinds of research could this include? How could the public be involved?</li><li>How could the public be involved in discussions about ethical involvement of animals in research?</li></ul></td>
<td></td>
<td>10</td>
</tr>
</table>

| Session | Summary | Learning aims | Learning outcomes | Activity instructions | Resources | Time |
|---|---|---|---|---|---|---|
| What is good research? | Who decides what makes research good, and what does 'good' mean? | To explore the concepts behind 'good' research and how everyone can be involved in these decisions | • Explain the concepts behind the 'Declaration of Helsinki', 'Good Clinical Practice' quality standard and how this applies to reviewing protocols<br>• Be able to apply concepts of critical appraisal to a real research proposal | • Ask people what good research looks like<br>• Ask if anyone knows the current way international ethics is currently codified – talk briefly of the history or ethics and refer to relevant resources<br>• Ask people to read the 'HEPATIC Phase I protocol' protocol and to see what they think (give 2 min depending on time). Mention we'll come back to this<br>• Optional pre-reading -<br>  ○ Read the abstract of this paper – any thoughts? A good paper about non-clinical research with impacts in self management – not all research has to be clinical<br>  ○ Read the abstract for this paper about patient involvement in setting outcome measures for arthritis<br>  ○ Read this short article: 'No research about me without me – Why researchers should welcome the patient's voice'<br>  ○ Read 'Incorporating patient preferences in the management of multiple long-term conditions: – it is about how people need to be involved in creating clinical practice guidelines – it is how the research is translated<br>• Make sure people know about the CASP resources http://www.casp-uk.net/casp-tools-checklists<br>• There are additional resources that you might find helpful or interesting | Resource 6: A brief history of clinical trials<br><br>Resource 7: A brief history of research ethics | **15** |

| Session | Summary | Learning aims | Learning outcomes | Activity instructions | Resources | Time |
|---|---|---|---|---|---|---|
| | | | | • Ask people to read the advert for LOMA in Activity 3<br>• So what was GOOD about the 'HEPATIC Phase I protocol' – make the point that as part of the team you are there to improve it, so always good to start with what is good<br>• What could be improved?<br>• Go through it in detail finding all the ethical problems with it<br>• This is critical appraisal (Resource 14) | Activity 3: Advert for LOMA<br><br>Resource 14: Questions to ask about research | |
| Applying the principles of critical appraisal | An opportunity to apply the principles from the previous sessions to real examples | Participants will have a chance to appraise a research proposal | • Be able to summarise the main skills and knowledge areas they are happy with and those they would like to develop for critical appraisal | • Ask participants 'What did you think about the other papers- did anyone read those?<br>• Ask how they found the experience of reading the GOUT trial?<br>• What did they find easy, what did they find difficult?<br>• Ask people to complete a Skills and knowledge grid (preview link) to help appraise their own skills (or if time is short do this as a discussion). They can make a copy here if they have a google account. | Resource 22: Skills and knowledge grid | **15** |
| Involved in improving services | Learn about how people can get involved in improving services | To explore how people can and should be involved in service design | • Participants can explain the national standards about involvement and how they can be involved | • What does getting involved in improving services and care means to them?<br>• Have you ever been involved in planning, design, delivery, measurement and evaluation of services?<br>• Who is involved in deciding the budget and what to spend it on – this is called 'commissioning'<br>• A crucial step of commissioning is the 'needs assessment' – this involves research – which is the best way to improve services- it's all connected | Resource 21: Involving people in improving services | **10** |

| Session | Summary | Learning aims | Learning outcomes | Activity instructions | Resources | Time |
|---|---|---|---|---|---|---|
| Working together | The principles of effective group working and communication | To explore practical best practice which can make working as part of a team or group more effective | Participants will be able to:<br>• explain the importance of the interactions within a group and the responsibilities of being a team member in a meeting<br>• explain why 'Terms of Reference' are important for collaborative working and how its structure operates | • Ask who has worked in teams or groups before?<br>• What makes group working effective?<br>• Work through the '6 rs' handout<br>• Talk about 'what are you doing to involve people' and ask them to appraise any organisation they are working with | Resource 8: Maslow<br><br>Resource 9: The 6Rs<br><br>Resource 10<br><br>Resource 11: What are you doing to involve people? | **15** |
| Summary and next steps | A chance to summarise the session and agree and next steps | Participants will have an opportunity to reflect on what they learned, what was useful and any further areas of development | Participants will be able to:<br>• explain what they have learned<br>• identify areas where they would like to develop knowledge and skills | • Does anyone have any reflections after the discussion we have just had?<br>• Has anyone learned anything useful<br>• Are there any areas people would like to develop their skills or knowledge in?<br>• Complete an action plan<br>• Does anyone have any actions they would like to share | Online Activity 4: Action plan<br><br>(create your own copy here) | **10** |

| Session | Summary | Learning aims | Learning outcomes | Activity instructions | Resources | Time |
|---|---|---|---|---|---|---|
| Evaluation and closing | Participants will be asked to complete an online evaluation form and the session will be closed. | | | **Suggested questions:**<br><br>1. Please describe the area/s of the event that you found most valuable/most enjoyable:<br><br>2. Please describe the area/s of the event that you found least valuable/least enjoyable and/or areas that could have been developed further<br><br>3. How was your experience of learning online? What worked well – what could have been improved?<br><br>4. How do you intend to apply what you learnt on the event? What will you do differently? What do you think will be the effect of this?<br><br>5. If you have any other comments or suggestions then please write them here or attach them: | | **5** |

# Resources

# Resource 1: Public Involvement in Clinical Trials

The National Health and Medical Research Council defines involvement as:

"research being carried out with or by consumers and community members rather than to, about or for them[1]'

The Australian Code for Responsible Conduct of Research states that 'appropriate consumer **involvement in research should be encouraged and facilitated by research institutions and researchers'**[2] although, appropriate is a subjective word and there are many interpretations.

The 'Statement on Consumer and Community Participation in Health and Medical Research' (NHMRC and Consumers' Health Forum of Australia Inc, 2002) **'seeks to encourage a different kind of participation, where consumers and researchers work in partnership with one another to shape decisions about research priorities, policies and practices.[3]'**

The National Health and Medical Research Council "Revised Statement on Consumer and Community Involvement in Health and Medical Research statement" also states:

"Active involvement of consumers and community members in health and medical research **benefits the quality and direction of research**. The vision for the Statement is: Consumers, community members and researchers will **work in partnerships based on understanding, respect and shared commitment to research that will improve the health of all Australians.** Consumer and community involvement is about **research being carried out with or by consumers and community members rather than to, about or for them**. It includes consumers and community members working with research funders to prioritise research, being involved in grant funding processes and providing advice as members of project steering groups. This is distinct from people who are the participants in research projects"

## International context

A report from the National Institute for Health Research stated:

"public involvement in research has had a variety of impacts, including impact on the research (at all stages and levels), on the members of the public who were involved, on the researchers, on participants, on community organisations and the wider community. It has also influenced whether the results of research have been used to bring about change."

1 http://consultations.nhmrc.gov.au/files/consultations/drafts/draftconsstatementconsultationversion140807.pdf
2 http://www.legislationreview.nhmrc.gov.au/_files_nhmrc/file/research/research-integrity/r39_australian_code_responsible_conduct_research_150811.pdf
3 https://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/r33.pdf

## Resource 2: Stories and facts about public involvement in research

All these stories are real but have been anonymised. Think about what these stories might mean and what you might learn from them. Please feel free to use them and add to the collection.

**Why we involve the public –** A researcher who spent his life researching arthritis was diagnosed with it towards the end of his career. He stated he'd spent his life researching the wrong thing. He was researching a cure when he should have been researching how to open jars. He should have been researching how to live with arthritis. The MS Society famously asked their supporters how they should spend their research budget and as a result they shifted their funding focus to curing and living with, rather than just curing.

**Public involvement in participant information is an ethical issue**

A 'Participant Information Sheet' (PIS) which had been through 'user testing' (involving the public to provide a lay perspective and improve it) produced a 'revised PIS significantly altered in its wording and layout'. This was compared with one that hadn't been revised. When given a written test, 66% of participants who read the revised PIS were able to show understanding of all aspects of the trial, compared with 15% of those reading the original version. Therefore the original PIS 'may not have enabled valid consent'.[4]

**All information needs to be as clear as possible** – A man's 2 year old daughter was in intensive care with advanced leukemia, doctors said she had a number of hours to live. While by his daughter's bedside, he was asked if he could leave the room for a moment and have a conversation. He was met by three doctors who sat him down at a table, all three on the opposite side to him. They wanted to recruit his daughter onto a clinical trial. He had to decide then and there if he would consent. He decided not to, because it felt too rushed. His daughter is now ten and doing well.

**The public will be involved, one way or the other** – A researcher who was leading a clinical trial into gene therapy on the back of the retina. While carrying out the trial, participants formed their own user group with no formal encouragement or financial support from professionals involved in the trial. They then began to give feedback to the trial organisers on how it was run and ways to improve it.This included changing the time of morning blood test appointments from 9am to 11am, as participants could then use their free bus pass. The result was that the trial retained many more participants, as the feedback made it more appealing to people involved. The researcher leading the trail was asked if they had written about the public involvement in their write up of the results. They said they hadn't, despite the fact it immeasurably improved the trial and quality of the results.

**Know your audience** - A Clinical Research Nurse based in Glasgow was doing quick study to work out how accessible local memory service appointments were for a individual living with dementia and their carers. The idea was to call the carer and ask them a few questions on the phone to help inform decisions on access. All the people being phoned had agreed to share their views for the study, but when the Nurse and her team set out to make the calls one afternoon, they noticed nobody was answering the phone, so they gave up. The next morning, everyone answered, and when they enquired as to why their calls had gone unanswered the afternoon before, a *very* common answer was "oh the news was on, so we don't answer the phone during that".

4 Reference Knapp et al. BMC Medicine 2011, 9:89 http://www.biomedcentral.com/1741-7015/9/89

# Resource 3: Why involve the public in research? How can it be done?

Involving the public in research can:

- Improving trust and public influence over research[5]
- Ensuring that research is conducted in an ethical, accessible and transparent way
- Help with developing grants and making grant applications[6]
- Help identify and prioritise issues, ensuring that research reflects the balance and diversity of priorities within populations[7]
- Avoiding wasting funds doing research that is not needed[8]
- Help improve design of trials[9]
- Lead to better recruitment to trials[10]

## Who is involved? What words are helpful?

It is important to explore these different terms. Do you really need 'patient' involvement, or just someone to check something is in plain English – or do you need someone with a very specific experience or condition to help inform your work.

Can anyone be involved – is the word 'public' helpful?

If you use the word 'consumer' – do the people you're talking about self-identify with this word?

INVOLVE state:

> 'Whilst all of us are actual, former or indeed potential users of health and social care services, there is an important distinction to be made between the perspectives of the public and the perspectives of people who have a professional role in health and social care services'[11.]

## Tasks – what will you ask people to do?

It is very important to reflect on the tasks that you will be asking people to do – and what skills, experience or knowledge that person might require. In addition, it's very important to always consider what support they might need. This might be learning and development, financial or emotional support – perhaps a buddy or mentor.

## Method and mode – how will you involve people

Consider what methods will be used when people are involved. Will it be facilitated groups, reviewing documents, completing surveys?

Consider the mode of communication – will it be face to face or online? How will these decisions affect who is included or excluded from being involved?

**Remember – involving people in codesigning all of the above will ensure that the involvement plan better suits people's needs**

---

[5] https://www.ncbi.nlm.nih.gov/pubmed/22809132
6 http://www.ncbi.nlm.nih.gov/pubmed/24118732
[7] https://researchinvolvement.biomedcentral.com/articles/10.1186/s40900-015-0003-x
8 http://www.sciencedirect.com/science/article/pii/S0140673613622291
9 http://www.sciencedirect.com/science/article/pii/S0168851009002929
10 http://researchinvolvement.biomedcentral.com/articles/10.1186/s40900-015-0008-5
11 http://web.archive.org/web/20160527051935/http://www.invo.org.uk/find-out-more/what-is-public-involvement-in-research-2/

## Which stage of the research cycle?

The public can be involved at every stage of the research cycle, from identifying topics, prioritisation, to funding, designing trials (improving recruitment), analysing data, dissemination and even translation.

| Stage | Why involve the public | How | Example |
|---|---|---|---|
| Identifying and prioritising | Involving the public in helping to identify and prioritise research allows them to influence what will be researched and lets researchers check that research priorities are the same as those of people who have the conditions being researched or who use relevant services. | Use a mixture of face to face and online tools to facilitate discussions with existing reference groups and networks.<br><br>This can include inviting the public to an event or researchers attending public and patient forums and events. | • In Australia, a Consumer Research Forum was held by Cancer Voices for members from around Australia. They used the 'global café' technique so that all 40 participants could discuss and log their priorities on five major cancer research topic areas. The outcome of this exercise has been used by Cancer Voices to alert researchers and funders to consumer priorities[12]. A peer reviewed paper was produced to inform other interested cancer research funders about what people affected by cancer would like to see researched[13].<br>• In the UK the James Lind Alliance facilitates Priority Setting Partnerships. These partnerships bring patients, carers and clinicians together to identify and prioritise the treatment uncertainties which they agree are the most important for research. |
| Funding or commissioning | Many funding organisations now involve members of the public in commissioning research. This gives a broader | • Involve members of the public in reviewing research proposals | • Applications for Cancer Council NSW Project Grant funding are first reviewed through the National Health and Medical Research |

12 http://web.archive.org/web/20160603024117/http://cancerforum.org.au/letter-to-the-editor/2015/november/cancer-consumer-involvement-in-research-in-australia/
13 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3532819/

| Stage | Why involve the public | How | Example |
|---|---|---|---|
| | perspective to the review process, by considering the issues that are important from a public perspective. | • Have a members of the public on research commissioning panels or boards<br>• Research grant applications<br>• Organisations representing groups or conditions commissioning research. | Council (NHMRC) peer review process and then by the Consumer Review Panel. The Consumer Review Panel assesses the remaining fundable applications based on specially designed consumer criteria<br>• After asking people affected by multiple sclerosis, the MS Society decided to fund research into improving the day-to-day lives of the people it affects, as well as biomedical research.<br>• A number of cancer research funding agencies, including Cancer Council NSW, Cancer Australia and others require researchers to describe in their research proposals the extent to which consumers are involved in their research.<br><br>Specifically, the requirement for consumer involvement in research may include the need to:<br>○ Discuss the extent to which relevant informed consumers have been involved during the development of a research proposal; and<br>○ Provide evidence within the proposal for ongoing consumer involvement in the proposed research.14 |

14 http://web.archive.org/web/20160525073652/http://sydney.edu.au/cancer-research/resources/consumer.php

| Stage | Why involve the public | How | Example |
|---|---|---|---|
| Designing and managing | Involving members of the public in the design of research helps to ensure that the research is relevant to the needs of people, helps ensure the research question and outcomes are clear and ensures the research method has thought about the needs of anybody participating in the research. | Involve the public in:<br>• Reviewing proposals and commenting on any potential difficulties in the design<br>• Developing research tools, information such as questionnaires, patient information sheets and consent forms<br>• Monitoring and managing the research process<br>• The selection process of staff and researchers | • The 'Workplace Impact of Supported **Employment** Study' involved service users in the design of study through a local group. The purpose was to investigate the impact of Individual Placement and Support in a mental health catchment area.<br>• **Biobanking** – Having members of the public and donors involved at every level, including a 'lay steering committee….who are themselves donors' results in 'a proportion of the participants being engaged in dynamic consent' which is more practical. 15 |
| Undertaking | Involving members of the public in undertaking research can mean that research is carried out by people with a personal experience of the area of research or with relevant knowledge of a particular culture. | Involve the public in:<br>• Gathering and reviewing documentary evidence<br>• Carrying out interviews and running focus groups<br>• Developing research tools and information<br>• Analysing and interpreting the data or results of research. | • The Macmillan Listening Study trained people affected by cancer to carry out research to identify the cancer research priorities of people affected by cancer<br>• **Research Buddies** - there are many variations on this, but essentially it is having members of the public, often people affected by a condition, paired with researchers helping motivate and enthuse them about their work. WEHI's system is leading edge work in Australia, supported by a Consumer Advisory Panel at WEHI |

15 http://www.researchinvolvement.com/content/1/1/3

| Stage | Why involve the public | How | Example |
|---|---|---|---|
| Analysing and interpreting | Why: Publishing linked data and results in the public domain allows others to analyse any findings and facilitates a range of people to give their time, scrutiny and perspective to the research | Involve the public in:<br>• Interpreting and commenting on results<br>• Analysing publicly available open data | • The University Of Western Australia founded a programme to support researchers, consumers and the community to work in partnership to make decisions about research development using linked data.<br>• Genes in space, Eyewire, Cell slider and Foldit all allow the public to access data and interpret it. |
| Disseminating | Why: Dissemination is critical is the knowledge gained from the research is to have an impact. Good dissemination can also help identify the need for further research in a particular area. | Involve the public in:<br>• Developing the dissemination plan<br>• Summarising the research findings in clear and accessible ways<br>• Presenting at conferences, speaking to patients, support groups and service providers<br>• Publication in open access peer-reviewed scientific journals<br>• Publishing on websites, writing to journalists, creating leaflets for waiting rooms or community centres. | The Eve Appeal sent a letter to everyone who took part in the UKCTOCS screening trial and offered them the chance to continue to receive updates. |
| Implementing | Why: Members of the public involved in research are often passionate to ensure that action happens as a result of the research and are often able to establish relationships with key agencies and policy makers. | Work in partnership to plan the implementation as early as possible. | Example: Service user researchers and a nursing researcher co-delivered training in therapeutic interventions to staff teams in a mental health trust (St George's, University of London) |

| Stage | Why involve the public | How | Example |
|---|---|---|---|
| Evaluating impact | By evaluating the impact of research and public involvement in research, you can help to build an evidence base and let others know about what worked well and what could be improved. | Involve the public in:<br>• How you are going to monitor and evaluate the impact of the research, and the public involvement in the research!<br>• Writing up (and publishing) an evaluation of the public involvement itself! | The UK Clinical Research Collaboration published a report of a project to evaluate patient and public involvement in research. |

This table is adapted from the resource 'Building Research Partnerships' – which can be downloaded for free here:

macmillan.org.uk/researchlearning

In addition, INVOLVE have a page of more resources which describe how you can involve people at each stage of the research cycle:

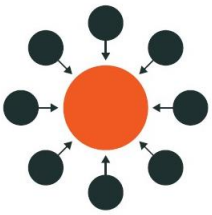
http://www.invo.org.uk/posttyperesource/where-and-how-to-involve-in-the-research-cycle/

## Resource 3.1: What is patient and public involvement?

Read the three descriptions of participation, engagement and involvement below. Do they make sense?

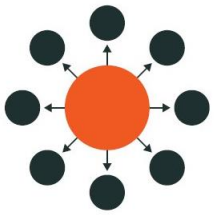
# What is Patient and Public Involvement?

Patient and Public Involvement (PPI) in research, is defined as **research carried out 'with' or 'by' patients and those who have experience of a condition**, rather than 'for', 'to' or 'about' them. Whilst engagement and participation are important ways of interacting with people with arthritis in research, we believe that involvement provides very influential and meaningful insight that is essential to anyone aspiring to improve the quality of life of people with arthritis.



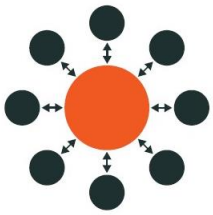
**Participation**

People take part in a research study.



**Engagement**

Information and knowledge about research is provided, and disseminated.



**Involvement**

Where members of the public are actively involved in research projects and in research organisations.

# Why we Involve People with Arthritis

By adopting meaningful patient involvement approaches to our research activities, we will increase the relevance of our work, enhance research excellence and help to ensure studies with patient participation are as safe, sensitive and ethical as possible.

# How we Involve People with Arthritis

We integrate patient insight into the charity via our patient insight partners (PIPs). We involve our PIPs in a number of different activities ranging from priority setting partnerships that steer strategy, to reviewing grant applications. When reviewing grant applications, PIPs contribute in parity to research experts, taking part in lay peer review and acting as integral members of our subcommittees. With this approach we gain relevance, but not at the expense of scientific excellence.

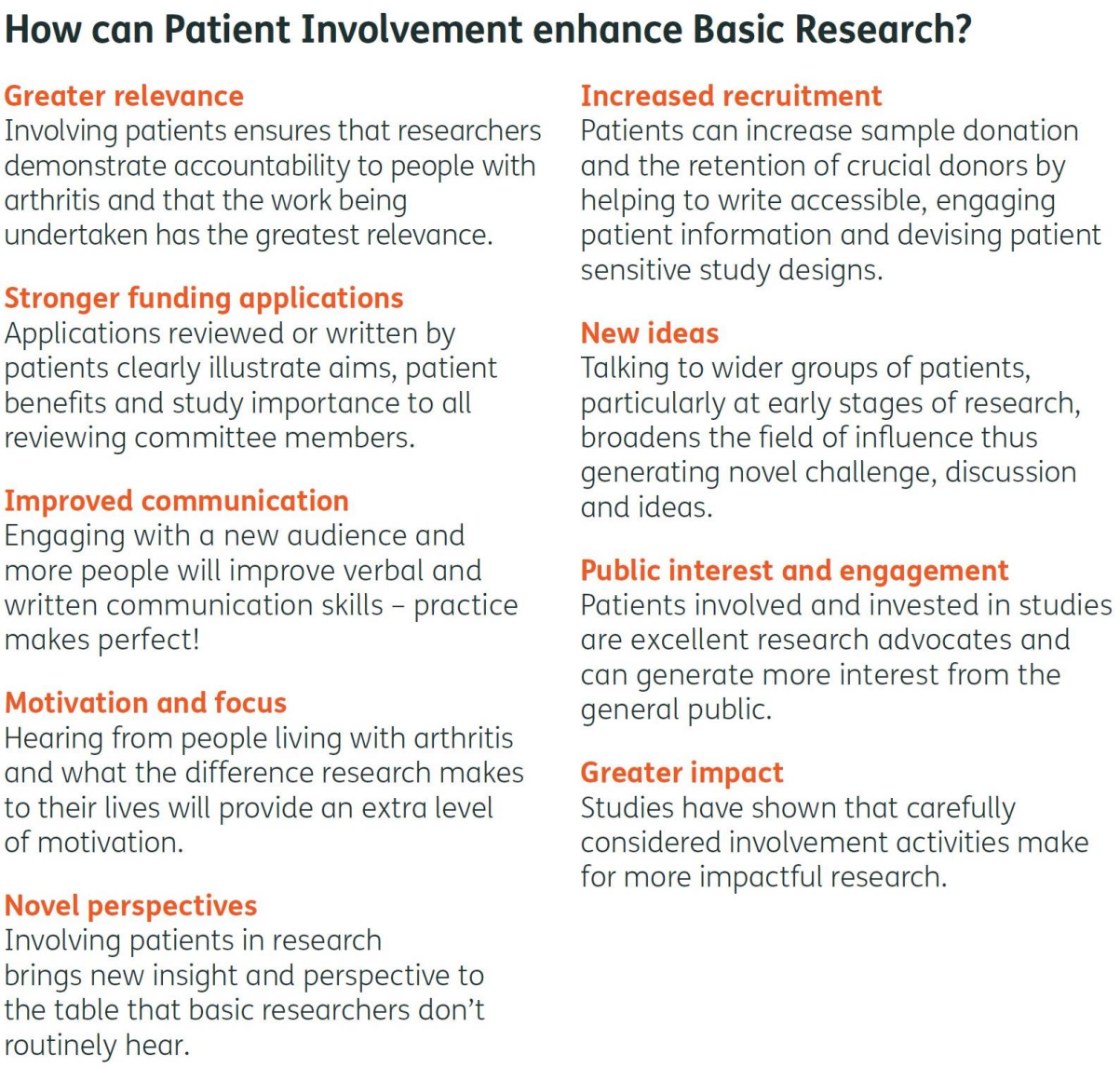
Taken from 'Patient and Public Involvement – a Researcher's Guide (Versus Arthritis)' [16]

[16] https://www.arthritisresearchuk.org/research/news-for-researchers/2017/july/patient-and-public-involvement_a-researchers-guide.aspx

## Resource 3.2: How can involving patients improve 'basic' research

'Basic' research can be thought of as 'foundational' – exploring knowledge that is the basis for all other discoveries and research – it does not mean it is simple!

Versus Arthritis created this summary of how patients can be involved in basic research:




Taken from 'Patient and Public Involvement – a Researcher's Guide (Versus Arthritis)' [17]

[17] https://www.arthritisresearchuk.org/research/news-for-researchers/2017/july/patient-and-public-involvement_a-researchers-guide.aspx

# Resource 4: Exploring the context

## Australian context

The National Health and Medical Research Council "Revised Statement on Consumer and Community Involvement in Health and Medical Research statement" says:

"**Active involvement of consumers and community members in health and medical research benefits the quality and direction of research.** The vision for the Statement is: Consumers, community members and researchers will work in partnerships based on understanding, respect and shared commitment to research that will improve the health of all Australians. Consumer and community involvement is about research being carried out with or by consumers and community members rather than to, about or for them. It includes consumers and community members working with research funders to prioritise research, being involved in grant funding processes and providing advice as members of project steering groups. This is distinct from people who are the participants in research projects"[18]

A recent review of public involvement by the National Institute for Health Research recommends that 'relevance' be one of the three measures of success of future public involvement in health and social care research.[19]

Relevance is defined as '**questions that reflect the interests and needs of patients, carers and clinicians'**[20]

### Australia & New Zealand Breast Cancer Trials Group

The Australia & New Zealand Breast Cancer Trials Group (ANZ BCTG) is the first collaborative cancer clinical trials group in Australia to establish a consumer advisory panel.

The role of the ANZ BCTG CAP is to:

- provide a consumer perspective on relevant issues about clinical trials including recruitment, patient information for informed consent, new trial protocols and ethical issues;
- improve recruitment to breast cancer clinical trials;
- advocate for women who are participating in clinical trials;
- raise community awareness of breast cancer clinical trials and research; and
- represent consumer views on behalf of the ANZ BCTG to media, Government, community, consumer and research funding forums.

CAP members review and provide comment on clinical trial protocols and particularly patient information and consent documentation. All members of the ANZBCTG CAP have had a personal diagnosis of breast cancer. It is this experience which helps us provide an important perspective to ANZBCTG research programs as well as help improve clarity and identify potential issues for the researchers to consider[21].

---

18 http://consultations.nhmrc.gov.au/files/consultations/drafts/draftconsstatementconsultationversion140807.pdf

19 http://www.nihr.ac.uk/get-involved/Extra%20Mile2.pdf

20 http://www.researchinvolvement.com/content/1/1/2

21 http://web.archive.org/web/20160607052049/https://consumerlearning.canceraustralia.gov.au/leonie_young

### International context

A report from the National Institute for Health Research stated:

"public involvement in research has had a variety of impacts, including impact on the research (at all stages and levels), on the members of the public who were involved, on the researchers, on participants, on community organisations and the wider community. It has also influenced whether the results of research have been used to bring about change."22

### Victorian context

The following are examples of research projects or organisations in the state of Victoria with examples of public involvement:

## Best-practice example: Melbourne Genomics Health Alliance

Melbourne Genomics Health Alliance brings together the clinical, research and teaching strengths among Victoria's leading hospitals and research organisations, with a vision to deliver genomic medicine into everyday healthcare. The Melbourne Genomics Health Alliance is 'committed to including patient and community views in our work' and established Community Advisory Group in January 201423.

The Community Advisory Group provides advice, direction and advocacy on matters of policy, design and evaluation of Melbourne Genomics. The Community Advisory Group:

- advises the Executive Management Committee and Program Team on patient and community views so they are recognised and reflected in planning and policy development
- makes recommendations on project design and evaluation to ensure inclusion of patient perspectives
- identifies and advises the Executive Management Committee on patient and community engagement
- advocates on behalf of the community for equity of access to genomic testing and information

The Committee won an award for their work and wrote a report which looked at the impact of their work.

### Academic context

A recent paper about involvement concluded that best-practice is to "Involve early - Patient input is often most impactful in the project formation phase. Researchers tend to have a focus on scientific questions and less on the wider context of disease. Patients can bring the perspective of what it is like to live with a disease, or several diseases/comorbidities...By having patient organisations, and their patients, as funded partners, a patient perspective was incorporated into even the earliest drafts of the project proposal and work plan"[24]

22 http://www.invo.org.uk/wp-content/uploads/2011/11/Involve_Exploring_Impactfinal28.10.09.pdf

23 http://web.archive.org/web/20160525073041/http://www.melbournegenomics.org/about-us/community-involvement

[24] http://www.researchinvolvement.com/content/1/1/5

## Resource 5: Attitudes

Sometimes a change in attitude involves individuals reflecting on assumptions and actively challenging these. Here are some helpful quotations that sum up some attitudes, taken from papers recently published in the new journal 'Research Involvement and Engagement':

- "There is a perception that patients either will not understand or would not be interested in the day-to-day operations of a research project. This often means that patients are given simplified and inaccurate explanations of how a project is progressing, what the challenges are and what the results mean. In reality, the more patients are involved in the day-to-day activities of the project, and the more they are informed about its progress, the more they can understand, contribute and positively impact."[25]

- Academic culture can often be very different from that of other spheres of work, and bringing lay representatives into the research arena helps to raise awareness of issues outside the academic culture box. This is particularly useful where researchers have moved through first and second degrees into doctorates and post-doctoral research in basic science. Lay members are more focussed on the practical aspects and outcomes of research and how it can affect patients and carers."[26]

- "The idea of patient involvement can be difficult for researchers as it does not adhere to the traditional "scientific method". The experiential knowledge of patients and the public, according to some, lacks the objectivity, verifiability, universality and rationality of scientific knowledge. However, it is now increasingly appreciated among researchers that patients' knowledge and experience is valuable for research and contributes to increasing the quality, relevance and appropriateness of research processes"[27]

- "A key feature of our model is that all research projects running through our facility are receiving involvement from a wide range of lay members. Individual lay members may get involved at a deeper level in specific projects, but they have broad involvement in everything that we do which means that on a monthly basis, there is always an opportunity for researchers and lay members to share opinions and ideas. This differs from many PPI models where individual projects are allocated one or two lay members whose involvement may go through peaks and troughs."28

- "Actually, it's surprising that it has taken us this long to focus on patient engagement because the results we have thus far are nothing short of astounding. If patient engagement were a drug, it would be the blockbuster drug of the century and malpractice not to use it." *Leonard Kish—Principal and Co-Founder of VivaPhi*[29]

[25] http://www.researchinvolvement.com/content/1/1/5

[26] http://www.researchinvolvement.com/content/pdf/s40900-015-0002-y.pdf

[27] http://www.researchinvolvement.com/content/1/1/4

28 http://www.researchinvolvement.com/content/1/1/3

29 http://www.researchinvolvement.com/content/1/1/4

# Resource 6: A brief history of clinical trials

## What are clinical trials?

Clinical trials are experiments that prospectively assign human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes[30]. Clinical trials may also be referred to as interventional trials. They are designed answer specific questions about biomedical or behavioural interventions including:

- new treatments (such as novel vaccines, drugs, dietary choices, dietary supplements, exercise and rehabilitation, psychological interventions, biological agents and medical devices)
- known interventions that warrant further study and comparison (e.g. surgery)

Clinical trials ideally generate data on safety and efficacy and are conducted only after they have received health authority and/or ethics committee approval in the country where approval of the therapy is sought.

## Early echoes

- An interesting experiment to test healthy eating is described in the Bible, complete with a planned experiment with both baseline and follow-up observations of two groups who either partook of, or did not partake of the intervention, which then resulted in a changed diet:

> "ten days; and let them give us pulse to eat, and water to drink. Then let our countenances be looked upon before thee, and the countenance of the children that eat of the portion of the king's meat: and as thou seest, deal with thy servants. So he consented to them in this matter, and proved them ten days. And at the end of ten days their countenances appeared fairer and fatter in flesh than all the children which did eat the portion of the king's meat. Thus Melzar took away the portion of their meat, and the wine that they should drink; and gave them pulse[31]"

- Persian physician Avicenna, in "The Canon of Medicine" (1025) gave similar advice for determining the efficacy of medical drugs and substances.[32]
- In the 9th-century, the Persian physician al-Razi compared the outcome of patients with meningitis treated with blood-letting with the outcome of those treated without it to see if blood-letting could help.[33]

## The first clinical trial: James Lind

James Lind conducted the first clinical trial in 1747 into the cure for scurvy in, which was a potentially lethal problem for sailors on long voyages. There were many competing theories as to effective cures to James Lind tested the various treatments.

Before beginning his comparison of six treatments for scurvy on board HMS Salisbury in 1747, James Lind took care to **select patients who were at a similar stage of this often lethal disease**; ensured that the patients had the same basic diet and also arranged for them to be accommodated in similar conditions.

---

30 http://www.who.int/ictrp/en/
31 http://www.gutenberg.org/files/10/10-h/10-h.htm#The_Book_of_Daniel
32 http://www.oxfordscholarship.com/view/10.1093/acprof:oso/9780195035681.001.0001/acprof-9780195035681
33 http://www.testingtreatments.org/wp-content/uploads/2012/09/TT_2ndEd_English_17oct2011.pdf#page=94

**Lind recognized that factors other than the treatments themselves might influence his patients' chances of recovery**[34].

He divided twelve sailors with scurvy into six groups of two. They all received the same diet but, in addition, group one was given a quart of cider daily, group two twenty-five drops of elixir of vitriol (sulfuric acid), group three six spoonfuls of vinegar, group four half a pint of seawater, group five received two oranges and one lemon, and the last group a spicy paste plus a drink of barley water. The treatment of group five stopped after six days when they ran out of fruit, but by that time one sailor was fit for duty while the other had almost recovered[35].

## Early randomisation

In 1854, Thomas Graham Balfour, an army doctor in charge of a military orphanage, showed how treatment groups could be created to ensure that like would be compared with like. Balfour wanted to find out whether belladonna protected children from scarlet fever, as some people were claiming. So, 'to avoid the imputation of selection' he allocated children alternately either to receive the drug, or not to receive it.[36]

## Modern Trials

Sir Ronald A. developed his 'Principles of experimental design' in the 1920s as an accurate methodology for the proper design of experiments. The important concepts in this book included:

- **randomization** - the random assignment of individuals to different groups for the experiment
- **replication** - to reduce uncertainty, measurements should be repeated and experiments replicated to identify sources of variation
- **blocking** - to arrange experimental units into groups of units that are similar to each other, and thus reducing irrelevant sources of variation;
- use of **factorial experiments -** efficient at evaluating the effects and possible interactions of several independent factors

The British Medical Research Council officially recognized the importance of clinical trials from the 1930s.

With the outbreak of the Second World War, the world was horrified by the things done in the name of 'science'. The aftermath is explored in 'A brief history of research ethics'

34 http://www.testingtreatments.org/wp-content/uploads/2012/09/TT_2ndEd_English_17oct2011.pdf#page=94
35 http://www.bruzelius.info/Nautica/Medicine/Lind(1753).html
36 http://www.testingtreatments.org/wp-content/uploads/2012/09/TT_2ndEd_English_17oct2011.pdf#page=94

# Resource 7: A brief history of research ethics

The word ‘ethics’ has a long and complex history. At the root is not one single definition, but an entirely subjective feeling that can best be summarised in English by the words ‘fairness’ or ‘justice’. While this feeling may be limited in expression by human language, there is evidence that this feeling is not exclusive to humans, with other animals displaying a sense of ‘fairness’ or desire for ‘justice’[37].

## Origins of a codified ethics in human research

After the crimes against humanity committed during the Second World War in the name of science, the response of the international community was to begin to codify what good research should look like, in order to prevent future atrocities.

**The Nuremberg Code** was the first international document to support the concept that "the voluntary consent of the human subject is absolutely essential". It emphasised:

- Individual consent
- informing participants of the risk-benefit outcomes of experiments

**The Declaration of Helsinki** was established in 1964 to regulate international research involving human subjects. Established by the World Medical Association it recommended:

- guidelines for medical doctors conducting biomedical research that involves human subjects.
- "research protocols should be reviewed by an independent committee prior to initiation"
- "research with humans should be based on results from laboratory animals and experimentation"

**The Belmont Report** was issued in 1978, commissioned by the United States of America in response to the infamous Tuskegee syphilis experiment. It summarises ethical principles and guidelines for research involving human subjects which are:

- for persons
- beneficence
- justice

## Modern day

**All Trials** - Research ethics includes ensuring that studies involving human beings are published and all results, positive and negative, disseminated. **It is still not currently compulsory that all results and data from trials involving humans is published**, meaning that unnecessary research could be repeated on humans or that finite resources are wasted. The All Trials campaign is an international campaign calling for all past and present clinical trials to be registered and their full methods and summary results reported - http://www.alltrials.net

37 https://www.nature.com/articles/nature01963

## Resource 8: Answering important questions using Maslow's 'hierarchy of needs'

Maslow's hierarchy claims that needs that are **low** in the hierarchy must be partially satisfied before needs that are **high** in the hierarchy can be prioritised. Think of a hierarchy as a pyramid, 'low' meaning a basic foundation.

The answers to the questions on the left lie at the very heart of good meetings. They've been placed in an order to approximate to the hierarchy. Discuss whether you agree with the questions being placed with the associated needs?

| | |
|---|---|
| 1. Will this be a good use of my time?<br>2. Why are we meeting anyway?<br>3. Are we going to accomplish something? Will this meeting help me make a difference? | **Self Actualisation**<br>To find self fulfilment and realise one's potential |
| 4. Will we stay on the topic or go off at a tangent? | **Creative needs**<br>To create symmetry, order, and beauty |
| 5. Is there an agenda? | **Cognitive needs**<br>To know, learn explore, find out |
| 6. What's expected of me?<br>7. What happened as a result of the last meeting?<br>8. Will we be making decisions and if so how? | **Esteem needs**<br>To achieve, to be competent, gain approval and recognition, self-confidence, independence |
| 9. Should I be here? Am I welcome? Do I feel I am being treated with respect? | **Belongingness and love**<br>To be loved, liked needed or accepted by others |
| 10. Where are the fire escapes?<br>11. Who are the other people? | **Safety needs**<br>To be free of danger physically and emotionally – a sense of security |
| 12. When will we take a break (e.g. to go to the toilet)?<br>13. Where is the food? When will we eat?<br>14. How long will this take? When are we leaving? (Will I need a strong coffee or a sleeping bag?) | **Physiological needs**<br><br>Food, water, shelter, sleep, excretion |


Questions adapted from Roberta's Rules of Order by Alice Collier Cochran Published by 2004.

## Resource 9: The 6Rs

When working with others in a group or on a project, it can be helpful to make sure the following are as clear as possible:

| |
|---|
| **Remit**<br>What is the purpose of the meeting/group?<br>Are there any terms of reference? Does everyone have a copy?<br>When they were last revised? Are they updated regularly? |
| **Role**<br>Is each member clear about why they are there?<br>What are people's expectations of you?<br>Do you or others ever find that you have conflicting roles?<br>What do others expect of you? |
| **Representative**<br>Are you seen as a representative?<br>If so, who are you supposed to represent? Do you have a constituency, a group of people whose views you aim to represent?<br>How are you supported to be a representative? How might you gather people's views?<br>How do you report back to them?<br>Are you there because of a personal experience? |
| **Responsibility**<br>What responsibilities do you or others have? (see terms of reference)<br>Who sets the agenda? Is this responsibility shared?<br>How are decisions made? How are they implemented? Who takes responsibility for reporting back and ensuring the wishes of the group are carried out? |
| **Relationships**<br>Does it feel like being part of a team, everyone working together?<br>Is there a sense of common purpose and goals?<br>Do you get along with each other? Do you know each other as individuals or are you strangers brought together by your roles? |
| **Readiness**<br>Are you ready to get involved? Have you considered your emotional readiness and any time commitments?<br>Have you received any training to help you prepare for your role? Have you thought about how can you maintain and support your wellbeing?<br>Do you know who or where you can go to for support regarding any of these issues? |

# Resource 10: Patient, consumer and public involvement

There are many things to think about when involving the public and patients in improving services – this document is intended to help ask the right questions for the right roles.

**How to use this resource**: Under 'Assumptions and barriers', read the questions and consider if these might be barriers to involving some people, and consider how you might overcome these. 'Learning needs and support' examines the role in more detail and asks questions about the support people might need support to develop.

**Be clear what you want**– do you want 'patient', 'user' or 'carer' involvement, a lay perspective or just anyone who can give their time? Consider who you might unintentionally exclude by using these terms and be clear what you mean by *engagement* or *involvement.*

| Assumptions and barriers | Role Description | Learning needs & support |
|---|---|---|
| • What commitment do you expect (time/financial implications)<br>• Have you asked people to think about their emotional readiness?<br>• Do you expect them to be reading and writing information and documents? Have you considered what formats might be appropriate?<br>• Are you assuming a good ability to speak and read English?<br>• Do you expect a certain educational background? | **Consumer/Lay Leader:** A person who speaks and acts on behalf of all members of the public, including patients and carers and who takes a leading role in representing other lay representatives. The role may involve holding people or organisations to account.<br><br>**Consumer/Lay representative:** a member of the public (not a professional) who is a representative. They must speak and act on behalf of others. They may be guided by lay leaders but will be expected to take direct action to ensure that they are informed and able to represent the views of others. | **How are they supported to be a representative?**<br>• How will they be gathering views?<br>• Will this involve research?<br>• Do they have a budget?<br>• Should they be paid?<br>• Is there admin and practical support (from an organisation?)<br>• Is there any training available?<br>**Who is already doing this?**<br>• Are there any opportunities for them to be involved in peer support or have or be a buddy?<br>• What can be shared with other organisations? (E.g. learning, resources)<br>**How are people involved?**<br>• Can people be involved in other ways? (e.g. is it face to face meetings? What can be done online, what cannot?) |
| • Are the people who have engaged with you the only people who might be interested? | **Interested and engaged consumers or members of the public:** People who know about and/or are interested in decisions being made, but may take no direct action other than giving feedback, being involved in a public dialogue or signing petitions. | **Could there be a need for translation?**<br>• Are there any groups or organisations who could support with this?<br>**Remember**: 'public dialogue' is not fully 'representative' but can give a strong indication of how the public at large feels |
| • It is easy to assume that people who are not engaged don't want to be.<br>• Often they won't even know how they can contribute or be involved<br>• Some may not be able to afford the time, caring responsibilities or travel. | **Uninformed, disengaged or disinterested members of the public:** people who, for what ever reason, are not engaged, informed or interested in influencing decision making or shaping the future of health and social services. | **A majority of the population are in this category**.<br>• What information or support might some people need to help engage them or move them into other roles?<br>• What might make people move back into this role? (e.g. not seeing direct improvements, or too much of organisational change?) |

**Remember**: roles are not always fixed, they are often just a way of articulating different things people can or should do. Tasks can be more focused. There is always a way for dedicated people to give their time and develop their skills, what ever the label or role description

## Resource 11: What are you doing to involve people?

How are the public involved in your work? This is an action-based approach to the spectrum of involvement, designed to aid discussion about **assessing current involvement and planning for future activities.** The pyramid gives an indication of how many people might be involved in each action.

| Actions | Involve people by… |
|---|---|
| **Innovating**<br>This includes prototyping, piloting, establishing and creating new ways of doing things. This can include anything from building partnerships or buildings. | **Supporting them to:**<br>• Design and carry out research<br>• Create solutions<br>• Implement ideas<br>• Learn from actions |
| **Managing, delivering and evaluating**<br>Working in partnership to manage ongoing activities. | **Having:**<br>• Clear roles and tasks for the public<br>• Elections and interviews when appropriate<br>• Clear and accessible accountabilities for all roles (including staff), groups and committees.<br>**Asking them to take actions such as:**<br>• Managing or overseeing actions, processes and procurement<br>• Directly delivering services or reviewing providers<br>• Evaluating actions, processes and outcomes |
| **Prioritising and planning**<br>Working in partnership to prioritise actions and plan implementation. | • Agreeing priorities in a clear, transparent way (this can include stopping certain actions)<br>• Having clear accountabilities for planning at all stages<br>• Having a transparent and adaptable budget |
| **Listening, responding and acting**<br>Actively seeking feedback, responding to ideas, compliments and complaints with actions. | **Asking them to help:**<br>• Interpret feedback<br>• Influence responses to ideas, compliments and complaints<br>• Asking for ideas for actions<br>This includes telling people what this action was, particularly those who have given feedback. |
| **Asking and discussing**<br>Asking people what they think, need and want and discussing it with them. | Inviting people from your intended audience or people you are trying to help to:<br>• Design **how** you will collect feedback and **interpret** the results<br>• Identify any potential barriers that might stop people from giving feedback. |
| **Telling**<br>Giving information about what you have done, are doing or are going to do. | • Sharing opportunities to be involved<br>• Asking people for ideas and support to share and disseminate what you want to tell people<br>• Ask for feedback about how you are sharing information and attempt to measure the impact. |

# Resource 12: Informed Consent

## What is informed consent?

Everyone taking part in a clinical trial must give 'informed consent', or have a parent or guardian or other legally authorised person give consent.

Informed consent means that potential participants **are given information about the key facts of a clinical trial, which allows them to make an informed decision before deciding whether or not to take part**.

Informed consent also means that participants are provided with information on new developments throughout the trial.

## Consent to entering a trial

You cannot be entered into a trial if you don't want to be. If you are asked to take part, you are free to say yes or no at any time. There should be no pressure on you to enter a trial. The research team will explain the details of the trial and provide written information to inform potential participants . The researchers will also provide a document, usually called a 'participant information and consent form', which includes details about the study. This information will include the trial's purpose, duration, required procedures, risks and potential benefits, alternatives, how confidentiality and wellbeing are protected, and contacts for further information.

Participants should be provided with the time to consider their options and find answers to the questions they need to make an informed decision as to whether they will consent to take part. If they consent, they will be asked to sign and date the consent form to document they understand the requirements of the trial and willingly agree to participate. Signing the consent document means that they are agreeing to take part in the trial and have understood what that will involve. The consent document is not a contract, and participants may withdraw from the trial at any time. If participants do withdraw from a clinical trial, the Australian Government states that 'the relationship between you and your doctor will not be affected'[38].

If there are any changes to the trial or to the protocol that may affect a participant's willingness to continue in a trial, they will be informed of that new information and asked whether they consent to remaining in the trial.The timeliness of the reconsent process will depend on the urgency of the information and impact to the participant.

## Giving consent for another person

Sometimes, a potential participant may be unable to give their own consent for participating in a clinical trial. Such people might include:

- those who may be temporarily unable to give consent, including unconscious patients
- those with a severe cognitive impairment, an intellectual disability, or a mental illness, including elderly patients with dementia; or
- people who are under 18 - a parent or guardian has to give legal consent who are not able to give consent. Depending on the child's age, their willingness to participate may be taken into consideration, although there is no formal guidance on how this should be assessed or documented.

38 https://www.australianclinicaltrials.gov.au/how-be-part-clinical-trial/informed-consent

In these circumstances, consent may sometimes be given by responsible family members, guardians or someone authorised by a court to act on behalf of the person who is not able to give informed consent. Different Australian states apply guardianship to clinical trials differently.

*Adapted from: 'Informed consent'* - https://www.australianclinicaltrials.gov.au/how-be-part-clinical-trial/informed-consent

## Resource 13: Regulating, registering and reporting clinical trials

### Australia

### Regulation and ethics

Human Research Ethics Committee (HRECs) play a central role in the Australian system of ethical oversight of research involving humans. HRECs review research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines[39] .

There are more than 200 HRECs in institutions and organisations across Australia. Many other countries have similar systems.

In undertaking this role, HRECs are guided by relevant standards. Standards include those in the National Statement on Ethical Conduct in Human Research (the National Statement) issued by NHMRC[40].

The Australian Code of Practice for the Care and Use of Animals for Scientific Purposes encompasses all aspects of the care and use of, or interaction with, animals for scientific purposes in medicine, biology, agriculture, veterinary and other animal sciences, industry and teaching[41] .

### Registration of trials

The Australian New Zealand Clinical Trials Registry (ANZCTR) is an online register of clinical trials being undertaken in Australia, New Zealand and elsewhere. The ANZCTR includes trials from the full spectrum of therapeutic areas of pharmaceuticals, surgical procedures, preventive measures, lifestyle, devices, treatment and rehabilitation strategies and complementary therapies. **Registration of a trial using ANZCTR is voluntary**, but if a registrant chooses to register a trial, certain fields are mandatory[42].

It is publicly owned and managed by a non-profit organization and is funded by an enabling grant from Australia's National Health and Medical Research Council (NHMRC)

In 2007 the ANZCTR was one of the first three trial registries to be recognised by the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) as a Primary Registry.

### International

Many clinical trials run by US organisations (that may have clinical trial sites in Australia) are registered on US NIH-sponsored clinicaltrials.gov. The ANZCTR and clinicaltrials.gov websites are the most common registers in which trials run in Australia will be registered.

---

[39] https://archive.is/2016.06.27-120451/http://www.nhmrc.gov.au/health-ethics/human-research-ethics-committees-hrecs

40 http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/e72_national_statement_may_2015_150514_a.pdf

41 https://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/r34.pdf

42 http://www.anzctr.org.au/Support/AboutUs.aspx

A search for clinical trials on Australianclinicaltrials.gov.au should extract trials registered on the ANZCTR and clinicaltrials.gov.

The World Health Organisation (WHO) states that 'The registration of all interventional trials is a scientific, ethical and moral responsibility[43]'

The WHO hosts the International Clinical Trials Registry Platform in order to 'ensure that a complete view of research is accessible to all those involved in health care decision making' and to 'improve research transparency that will ultimately strengthen the validity and value of the scientific evidence base'[44].

The WHO also gives each trial a Universal Trial Number (UTN) 'to facilitate the unambiguous identification of clinical trials'[45]. The UTN is not a registration number.

While all clinical trials must be registered, it is not a requirement that all the data or results from these human trials are shared. All Trials (http://www.alltrials.net) campaigns for this and explains[46]:

> "The results of around half of all clinical trials have never been published. Failing to publish results means the people who make decisions about medicines don't have full information about the benefits and risks of treatments we use every day"

**Sign the petition calling for all trials past and present to be registered, and the full methods and the results reported**.

http://www.alltrials.net/petition

+AllTrials

43 http://apps.who.int/iris/bitstream/10665/76705/1/9789241504294_eng.pdf
44 http://www.who.int/ictrp/en/
45 http://www.who.int/ictrp/unambiguous_identification/utn/en/
46 http://www.alltrials.net/news/the-economist-publication-bias/

# Resource 14: Questions to ask about research

Questioning everything is at the root of the scientific understanding, that's what gives us knowledge. Good research attempts to answer questions using a rigorous method to give results.

**Critical appraisal** is a way of looking at published or reported research and **asking questions about the validity of the methods, the results and how published findings can be acted on**.

Below are some basic questions to ask of any research before it moves on from the design stage. When answering these questions, try to start with what is good, and then move onto what could be improved.

**Ethics –** Are the participants being recruited in an acceptable way, and is there likely to be sufficient numbers for recruitment? Is a vulnerable population involved? How is privacy and confidentiality maintained? Is it possible to have informed consent? What is the process for consent, if applicable? Are participants paid and is this relevant? Are participants exposed to unnecessary risk? Have the benefits been described in an appropriate way? Are the exclusion criteria appropriate or too excessive? (e.g. gender, age or being pregnant are common exclusion criteria)

**Need** – Does the research question address something of importance to the public and patients? Does it look at clinical need or an uncertainty about current treatment or services?

**Public involvement** – Do you think the public and consumers have been involved in identifying the need for the **research**, the design of this research or any other stages? Is there any budget for public and consumer involvement? Is there any evidence of public involvement?

**Research method –** is the research question clear? Is the method valid? Do you need more information to answer these questions? Is the research new or has it been done before (e.g. has a systematic review been done)? Are the statistical methods appropriate? Will participants or the public be involved in data analysis?

**Translation –** is it clear how this research could be useful? If not, how could it be better explained?

**Research Funding** – Who is paying for this research, is there a conflict of interest? Is the cost of this research justifiable when compared with other priorities? Who owns the findings, data and the results (e.g. intellectual property)?

**Dissemination -** Will the results and data be published? Will this be publicly accessible (and open access)? (this may help avoid research being repeated). Will any of the successes of involving the public be shared? Will participants be provided copies of results?

---

The additional questions below can be more helpful to ask for clinical research:

**Patient experience** – what issues might there be? Will this potentially improve the experience of future patients?

**Information** – How is information presented to potential participants? What is good, what could be improved? Does this affect ability to give informed consent? Are the risks and benefits clear? Is the timescale and commitment clear?

**Training** – How are the researchers qualified for the roles they will undertake in the project?

**Registration and data storage**- How is data collected and stored? Will the trial be publicly registered?

For more detailed information on critical appraisal, find some free resources from the Critical Appraisal Skills Programme at: http://www.casp-uk.net

## Resource 15: Influenza, drugs, trials, data and evidence

| Timeline | What happened |
|---|---|
| **1918** | 500 million people across the world were infected by the 1918 flu pandemic and between 50 to 100 million are killed. One third of the world's population was infected and 3-5% killed. In Australia, 12,000 were killed. This makes it one of the deadliest natural disasters in human history. |
| **1920s-90s** | The influenza is described by some historians as the 'forgotten pandemic'[47] |
| **1990s** | News about bird flu and other pandemics in the 1990s onwards renews public awareness and concern about influenza outbreaks. |
| **1996** | "Oseltamivir" discovered by scientists using shikimic acid, an extract of Chinese star anise. *Oseltamivir is absorbed by the liver, it is processed and acts as an inhibitor for an enzyme involved in the reproduction of the virus.* 20 year patents relevant to Oseltamivir were sold to Roche and they name it 'Tamiflu'. |
| **1999** | In the USA, the Food and Drug Administration approved Oseltamivir for treatment of influenza in adults based on two double-blinded, randomized, placebo-controlled clinical trials. The trials were sponsored by Roche[48.] |
| **2005** | Oseltamivir was widely used during the H5N1 avian influenza epidemic. Governments around the world, including Australia and the UK stockpiled the drug.<br>The Australian government currently has a stockpile worth $192 million and the USA has spent more than $1.3 billion[49.] |
| **2006** | A Cochrane review raised controversy by concluding that oseltamivir should not be used during routine seasonal influenza because of its low effectiveness, stating it does 'not prevent infection or interrupt voidance of viruses from the nose'[50] |
| **2009** | The public and Governments around the world accept "some drug companies have airbrushed out bad results by not publishing them, which could result in a drug appearing to work better and more safely than it does in reality"51. Drug companies may sell the public drugs which have been approved based on evidence which they have selected themselves for publication. Often, even regulators have not seen all the information about human clinical trials. The "entire ecosystem of drug evaluation and regulation is deeply flawed"[52.] |
| **2010 - 2012** | Cochrane are denied Roche's full clinical study reports. |
| **2013** | 'All Trials' is launched and calls for 'all past and present clinical trials to be registered and their results reported' and data to be shared openly. |
| **2014** | Cochrane reviews all the previously un-released clinical study reports (detailed documents from the commercial sponsors of the trial). The reports involved more than 24,000 people. The review highlights that oseltamivir (and similar compounds) are not proven to 'reduce hospitalisations and serious complications' and 'lead to harmful effects that were not fully reported in the original publications'. [53] Deliberate publication bias made Tamiflu look 'better than it really was'.[54] |
| **2016** | Roche patents expire, anyone can make the drug without a paying licensing. |

**At present, it is still legal for researchers and pharmaceutical companies to withhold data from human clinical trials.**Sign the campaign at alltrials.net


47 America's Forgotten Pandemic: The Influenza of 1918, Crosby, 2004
48 http://www.accessdata.fda.gov/drugsatfda_docs/nda/99/21087_Tamiflu.cfm
49 http://www.news.com.au/lifestyle/health/government-spends-192-million-stockpiling-roche-drug-tamiflu/story-fneuzlbd-1226880199762
50 http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001265.pub2/abstract;jsessionid=CDCD7EF42B4D1949A23186C55FADEA50.f02t01
51 http://www.theguardian.com/business/2015/may/18/drug-trials-firm-to-challenge-plans-for-greater-transparency-over-results
52 http://www.bmj.com/content/348/bmj.g2630
53 http://community.cochrane.org/features/tamiflu-and-relenza-getting-full-evidence-picture
54 http://news.sciencemag.org/biology/2015/01/tamiflu-helps-newest-study-long-running-debate-says

## Resource 16: What did open data ever do for us?

Australia is one of the leading countries in the world for open data. Open data is publicly released raw data (for example all collected data, not statistics), often from the government or public services, which is made available to everyone so they are free to use or reuse it any way they like. While it can be read by individuals, for example in a spreadsheet, it is primarily designed to be 'machine-readable', so it can be inserted directly into computer programmes (written by those inside or outside government).

The Australian Government states that open data 'has intrinsic economic and social value, often in ways not foreseen by those that collect it. With appropriate consideration of commercial, privacy and security sensitivities, there is mounting evidence indicating that the public release of government-held data, in easily shared and readable formats, can fuel business activity, increase public sector efficiency, and provide better support for evidence-based policy development'[55].

Similarly the UK Government has made releasing open data a priority because[56]:

- It makes the government more accountable to citizens and strengthens democracy (for example DFiD's aid tracker)
- It brings us better public services
- It feeds economic and social growth

What brings open data to life is how people use it – the positive potential for collecting and analysing this data is enormous.

### What is Linked Data?

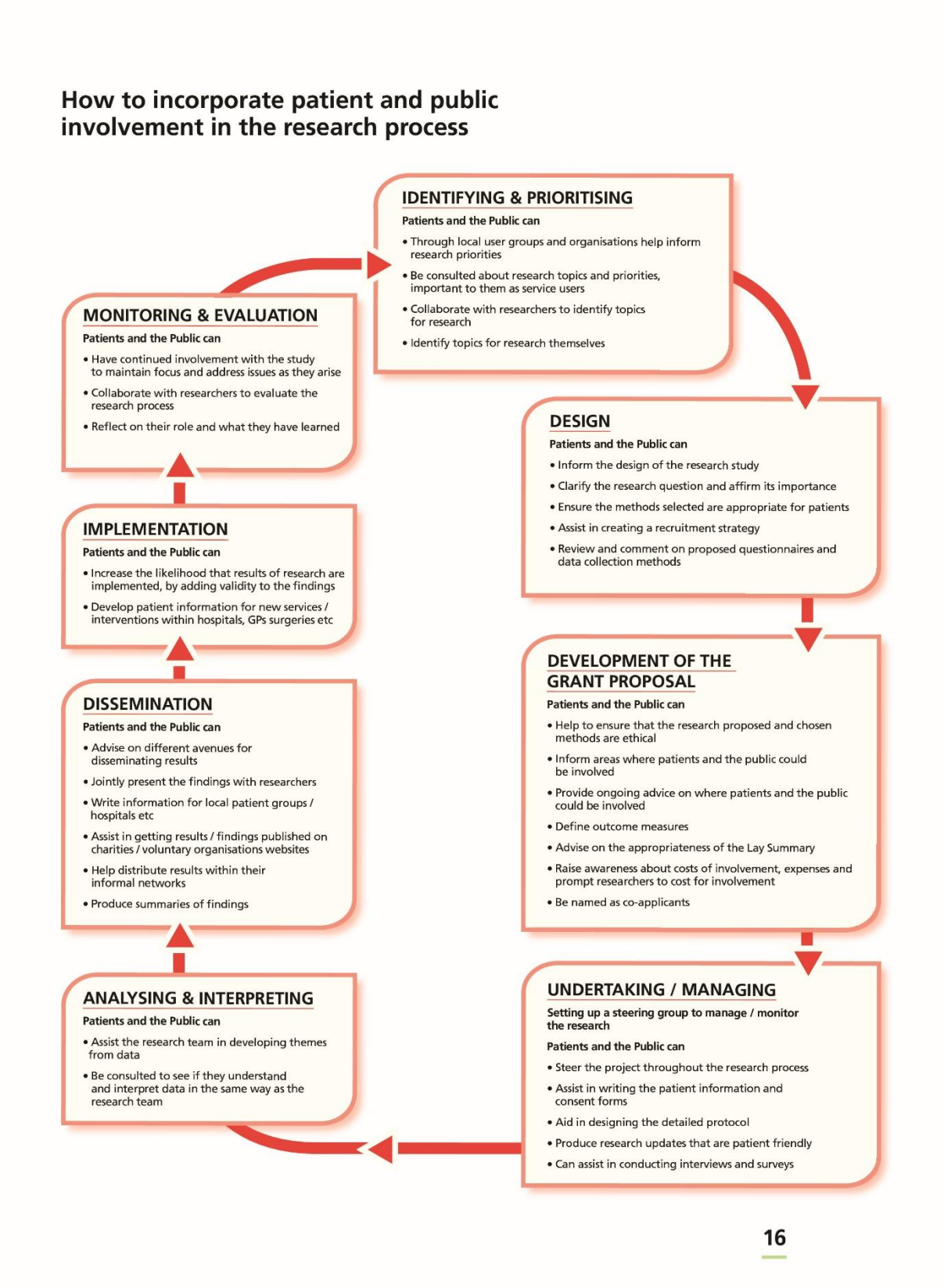
Sir Tim Berners-Lee's original vision of the world-wide web he designed was that it should also be used to publish, share and link data.

The Linked Data Web is not just about connecting datasets, but about linking information at the level of a single statement or fact. The idea behind the Linked Data Web is to use uniform resource identifier or URIs (these are like the uniform resource locators or URLs you type into your browser when going to a particular website) to identify resources such as people, places and organisations, and to then use web technology to provide some meaningful and useful information when these URIs are looked up. This 'useful information' can potentially be returned in a number of different encodings or formats, but the standard way for the linked data web is to use something called RDF (Resource Description Framework)[57].

## Consider: How might open and linked data might change the future of clinical trials?

55 http://web.archive.org/web/20160627052540/https://toolkit.data.gov.au/index.php?title=Policy
56 http://web.archive.org/web/20160627052656/https://data.blog.gov.uk/2013/10/29/what-did-open-data-ever-do-for-us/
57 http://web.archive.org/web/20160627053102/https://data.gov.uk/blog/what-linked-data

# Resource 17: Public involvement in the research cycle




Adapted with kind permission from Patient and Public Involvement in Health and Social Care Research: A Handbook for Researchers by Research Design Service London

# Resource 18: Areas for public involvement in research

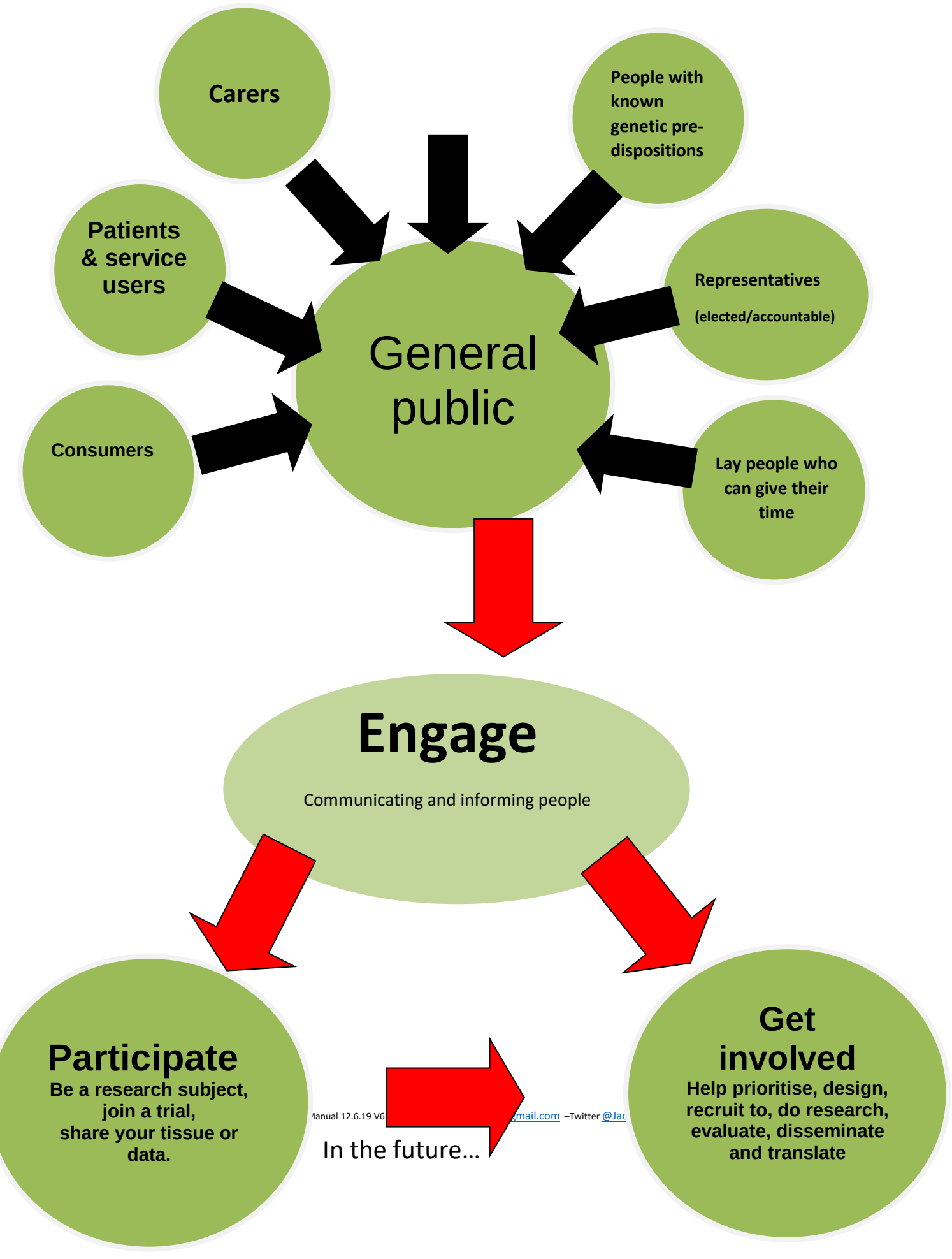
This table summarises the ways that the public and 'consumers' can be involved in different kinds of research. Can you think of any additional ways the public, consumers or patients could be involved?

| Type of research | Key characteristics | Potential areas of consumer involvement |
|---|---|---|
| **Bio Medical** | Laboratory-based<br>Complex<br>Controlled experimental designs<br>Molecular, cellular | • ethics<br>• member of a steering committee<br>• member of the project team<br>• communicating results broadly, in ways that are meaningful to consumers and community members |
| **Clinical research** | Laboratory based and/or human subjects<br>Controlled experimental<br>Designs<br>Quantitative methods | • ethics<br>• ownership or access to human tissue samples<br>• identifying areas for further research<br>• advocacy<br>• communicating results to participants and wider community in consumer-friendly ways<br>• member of a steering committee<br>• member of the project team |
| **Public health/ Population Health research** | Study of communities or populations<br>Social setting<br>Focus on epidemiology, health promotion and prevention, social and behavioural sciences, population based health interventions<br>Quantitative and qualitative methods | • identifying gaps in current knowledge<br>• identifying need<br>• contributing consumer focussed research<br>• advocacy<br>• informing policy development<br>• assisting/collaborating in research processes<br>• networking support and liaison<br>• communicating results<br>• translating results into practice<br>• member of a steering committee<br>• member of the project team |
| **Health Services, Health Economics & Social research** | Study of health-related institutions, including their operation within the broader system<br>Systems/policy focus<br>Complex social settings<br>Quantitative and qualitative methods | • identifying breakdown in systems<br>• feedback about quality, relevance and appropriateness of services<br>• collaboration in research processes<br>• contributing consumer focussed research<br>• research subjects<br>• member of a steering committee<br>• member of the project team<br>• providing consumer perspective on system issues<br>• networking support and liaison<br>• advocacy<br>• communicating results<br>• implementing results |

This table was taken from 'Areas for consumer involvement in research'[58], which was adapted from 'National Health and Medical Research Council [NHMRC] and Consumers Health Forum of Australia [CHF]. 2004. Resource Pack for Consumer and Community Participation in Health and Medical Research'[59]

58 http://web.archive.org/web/20160607053822/https://consumerinvolvement.canceraustralia.gov.au/assets/involve/files/doc-lib/accessible/researchers/r5.3-17_guide_areasconsumerinvolvementresearch.pdf
59 https://www.nhmrc.gov.au/guidelines-publications/r22-r23-r33-r34

Resource 19: Diagram of engagement, participation and involvement in research



## Resource 20: Common research terms

You may hear the following terms used often in research. Read the terms below and think about how these might be relevant to any kind of research you know about.

| Term | Definition |
|---|---|
| follow-up | Monitoring a person's health over time after an intervention. This includes keeping track of the health of people who participate in a clinical study or clinical trial for a period of time, both during the study and after the study ends |
| **Loss to follow up** | Where there are no results from certain participants on a trial (e.g. people who leave a trial) |
| **Exclusion/inclusion criteria** | Any criteria that would include or exclude someone from research (e.g. gender or age) |
| **Intervention** | This word is often used to describe what the research is testing or trying out. It could be a drug, a new kind of treatment pathway or something as simple as a massage. |
| **Trial arm** | Trials might have multiple 'arms' which are groups which are being tested simultaneously. One group will always be the 'control' group. This group has nothing different done to them than any other patient – they will often give results similar to the baseline measure. With drugs, the control group will often be given the 'placebo'. Different arms might start interventions at different times. Sometimes, trial managers switch which trial arm patients are on. They may or may not know when this happens. |
| **Blinding** | This is where the participant does not know which arm of the trial they are on, but the clinician does. 'Blinding' is not always possible (e.g. research into the benefits of massage) |
| **Double-blinding** | This is where neither the participant or clinician knows which arm of the trial they are on. Trial managers will always have records of who is on which arm, but may authorisation to 'unblind' a patient. |
| **Baseline measures** | These are the 'baselines', 'starting points' or 'benchmarks' which are objective measures which outcomes can be judged against. |
| **Outcome measures** | These are the outcomes that are measured at the end of the research, they must be the same as the baseline measures. |

| | |
|---|---|
| **Confounding factors** | A confounding factor is anything which might have influenced the trial that was unplanned. For example, 'everyone on the trial caught the flu during the trial' or 'there was a transport strike and people couldn't get in for bloodtests'. A confounding factor would not be something caused by the trial. |
| **Randomisation** | This is where patients are randomly allocated to a trial arm. Imagine someone flipping a coin. |
| **Sample size** | How many people were involved in the trial |
| **Bias** | Bias is an inclination to present or hold a partial perspective at the expense of (possibly equally valid) alternatives. Good questions to establish bias are:<br>• '**has all the raw data been published**, or just an interpretation of what the data meant?'<br>• '**who has funded this research**? Would the result be favoured by the funder and create a conflict of interest? (see this systematic review showing this effect has very real implications for research outcomes[60])<br>There are many different kinds of bias – with research suggesting that the human brain is susceptible to many different errors in processing data that effects research of all kinds[61]. This is called 'cognitive bias' – which may lead to<br>• perceptual distortion<br>• inaccurate judgment<br>• illogical interpretation<br>Some of these are referred to as:<br>• selection bias – data selected not appropriate<br>• recall bias – memory affects data<br>• detection bias – method of detection affects data |

[60] https://web.archive.org/web/20180309051628/http://www.bmj.com/content/326/7400/1167
[61] https://web.archive.org/web/20180309050838/https://www.nature.com/news/how-scientists-fool-themselves-and-how-they-can-stop-1.18517

| | |
|---|---|
| | Other cognitive biases are a "by-product" of human processing limitations (there is a physical limit to what the brain can process). |

# Resource 21: Involving people in improving services

The Australian Commission on Safety and Quality in Healthcare developed the National Safety and Quality Health Service (NSQHS) Standards to 'drive the implementation of safety and quality systems and improve the quality of health care in Australia'[62]. The eight NSQHS Standards are intended to provide a nationally consistent statement about the level of care people can expect from health services.

## Partnering

Standard 2 is called 'Partnering with Consumers' and is reads as follows[63]:

> 'Leaders of a health service organisation develop, implement and maintain systems to partner with consumers. These partnerships relate to the planning, design, delivery, measurement and evaluation of care. The workforce uses these systems to partner with consumers.'

The Standard states that there are 'mutually beneficial outcomes' by having people involved as partners in 'planning, design, delivery, measurement and evaluation of systems and services' as well as being partners in 'their own care, to the extent that they choose'.

## What is getting involved in service improvement?

Getting involved in improving services is[64]:

- the 'active involvement of service users', not their passive involvement as recipients of services or information.
- It is based on the principles of services 'for us, by us'

It is not[65]:

- 'us' versus 'them' – it's about how we can all work together for the best outcome
- another avenue to complain. There are specific channels of communication for complaints
- a chance to tell your story to as many people as possible.

It's about how to learn from your story and affect change.

## Feedback, ideas, compliments and complaints

While it is best-practice to make it clear how people can give feedback etc – it is not always obvious.

Patient Opinion is a not-for-profit organisation which has a platform which allows people to give feedback on 'what was good and what could be improved, say thanks or call for change - we'll pass your stories to the people in the health services who can make a difference.'

https://www.patientopinion.org.au/

## Remember - feedback saves and improves lives!

[62] https://www.nationalstandards.safetyandquality.gov.au/
[63] https://www.nationalstandards.safetyandquality.gov.au/2.-partnering-consumers
[64] https://web.archive.org/web/20110322210213/http://www.user-involvement.org.uk/about.php
[65] https://archive.org/details/ImprovingCancerServicesEnglandMAC1371

## Resource 22: Skills and knowledge grid

Knowledge is information you have in your head; a skill is the ability to use knowledge to achieve something.

| Skills | Knowledge |
|---|---|
| **Skills I already have** (for example driving, speaking English) | **Knowledge I already have** (for example a knowledge of my community or local information resources) |
| **Skills I have that I would like to develop** (for example talking to people affected by certain conditions) | **Knowledge I would like to develop** (for example an understanding of certain conditions and the treatments available) |
| **Skills I don't have but might need** (for example using the internet to communicate) | **Knowledge I might need** (for example a knowledge of funding opportunities) |
| **Skills I would be confident in helping others learn** (for example, reviewing funding applications) | **Knowledge I would be confident in sharing with others** (for example, a good route for a bike ride) |

Activity 1: Match the definitions to the letters

**Action research**

**Systematic reviews**

**Randomised controlled trial**

**A case control study**

**Translational research**

**Qualitative research**

**Laboratory research**

**A cohort study**

# Activity 1: Research Definitions

**A.** Research done in an environment (a laboratory) in which the team are able control and simulate clinical conditions or situations.

This research may include animal experiments or computer modelling.

**B**. Research that seeks to understand the experiences that people have in their lives. It captures knowledge that cannot always be counted in numbers.

It may be conducted by interviewing or observing people, using questionnaires or by reviewing case notes or diaries.

**C**. The researcher gains information about a particular problem or situation with the assistance of those who participate in the research.

It looks for solutions by carrying out 'an action' which is then reviewed to see whether it has addressed the problem. The process will be repeated until a satisfactory solution is found.

**D**. Research that studies a group of people who are free from disease but have been exposed to a potential cause of that disease.

These people may be compared with a control group that is similar but has not been exposed to the potential causal factor/s. Groups are followed up into the future to see what happens.

**E.** Research in which participants are randomly allotted or assigned to one of two groups.

One is the research group receiving an intervention, and the other is the control group receiving conventional treatment, no treatment or a placebo. Participants in both groups are monitored to see if any differences emerge.

**F.** Research that studies a group of people with a particular disease (an outcome of interest).

Researchers look back in time to see what those people may have been exposed to in order to identify possible causes of the disease. This is compared with a suitably matched but unaffected group.

**G**. A review of all the research studies that have been conducted into a particular topic where they have been systematically identified, appraised and then the results summarised according to pre-determined criteria.

This is usually carried out with randomised controlled trials but could also be used with other types of research studies.

**H.** A term used to define

research to test new treatments and diagnostic procedures for all diseases.

Research begins in the laboratory and covers all stages of experimentation up to and including transfer to 'first in human' clinical testing. Sometimes known as ''from the bench to the bedside''

**Activity 1 answers: Research Definitions**

**A Lab research:** the researcher has total control over the environment and what happens to the sample.
**B. Qualitative Research:** Is the room warm enough?, each of you will have a different answer depending on how you feel and if asked to judge it from 1 to 10 will probably have a range of answers.
**C. Action Research:** when the water was contaminated in a reservoir the scientists needed to work out how to destroy the bug and make the water safe again so they tried various ways of treating the water e.g. did that work, yes/no, why, try this, what did that do, try this, etc.
**D. Cohort Study** (forward arrow) the Chernobyl radiation leak. Those exposed to radiation have been monitored to see the effects alongside another similar group not exposed. The study is to see what are the effects of the exposure compared to the control group.
**E. Randomised Control Trial:** two groups of people, of a similar mix of age, sex, disease etc are compared when testing a new treatment on one group against the current treatment on the other. Randomization allows the results to be as impartial as possible. Most clinical trials are Randomised Controlled Trials (RCT's).
**F. Case Control Study:** a group of young asthma sufferers were investigated to see if living in a damp house affected/caused the asthma. Scientists looked back at the life of each child to see if they could identify similar conditions that would help them find a cause that matched most/all of them.
**G. Systematic Review:** Systematic reviews compare all relevant randomised controlled trials in health care or all comparable kinds of research. For example, in 1993 the Cochrane Collaboration led a review that compared similar research that had been done around the world to determine how effective giving steroids to premature babies was as all previous trials had been inconclusive. The review compared all similar trials and concluded steroids saved lives.
**H. Translational research:** Also known as ''from the bench to the bedside'' this describes the process of designing/discovering a treatment in a laboratory and then the process it goes through till it is tested on humans in clinical trials. You ''translate an idea into an action''.

## Activity 2: Stages and phases of research

Put the stages in the right order:

**Analyse and interpret data**
**Collect data**
**Commission or fund proposals**
**Design research**
**Disseminate**
**Evaluate impact**
**Identify topics**
**Implement or translate findings**
**Manage research**
**Prioritise topics**

| Stage number | Stage of the research cycle |
|---|---|
| **1** | |
| **2** | |
| **3** | |
| **4** | |
| **5** | |
| **6** | |
| **8** | |
| **9** | |
| **10** | |

**Phases of a clinical trial**

See if you can put the phases on the next pages in the right order:

| Phase | Letter |
|---|---|
| Pre-Clinical | |
| 0 | |
| I | |
| II | |
| III | |
| IV | |

**Questions to discuss:**

- How could the public be involved in each of these stages?
- Which stage might you want to consider specifically involving patients with relevant experience and why?
- Phase Y talks about different types of research to evaluate research. What kinds of research could this include? How could the public be involved?
- How could the public be involved in discussions about ethical involvement of animals in research?

**Phase Y**

| Primary goal | Typical number of participants |
|---|---|
| This phase gives no data on safety or efficacy, instead using single subtherapeutic doses of the study drug to a small number of subjects to gather preliminary data on the agent's pharmacokinetics (what the body does to the drugs) and increasingly, pharmacogenomics. Drug development companies carry out this phase decisions to be based on relevant human models instead of relying on sometimes inconsistent animal data. | 10 people |

**Phase Z**

| Primary goal | Typical number of participants |
|---|---|
| Extensive pre-clinical studies are carried out. These involve in vitro (test tube or cell culture) and in vivo (animal) experiments using wide-ranging doses of the study drug to obtain preliminary efficacy, toxicity and pharmacokinetic information. Such tests assist researchers in deciding whether a drug candidate has scientific merit for further development as an investigational new drug Testing of drug in non-human subjects, to gather efficacy, toxicity and pharmacokinetic information | No participants (*in vitro* and *in vivo* only) |

**Phase U**

| Primary goal | Typical number of participants |
|---|---|
| This phase is designed to assess the effectiveness of the new intervention against current standards of care and, thereby, its value in clinical practice. It aims to test interventions on patients to assess efficacy, effectiveness and safety, and in some cases the economic and quality of life benefits. Around 50% of drug candidates either fail during this phase or are subsequently rejected by the national regulatory agency[2]. | 1000-5000 |

**Phase X**

| Primary goal | Typical number of participants |
|---|---|
| **This phase is the first stage of testing in human subjects. This phase is designed to assess the safety (pharmacovigilance), tolerability, pharmacokinetics, and pharmacodynamics of a drug. These trials are often conducted in a clinical trial clinic, where the subject can be observed by full-time staff. These clinical trial clinics are often run by contract research organization (CROs) who conduct these studies on behalf of pharmaceutical companies or other research investigators. Phase I trials most often include healthy volunteers. However, there are some circumstances when patients are used, such as patients who have terminal cancer or HIV and the treatment is likely to make healthy individuals ill. There are different kinds of phases at this stage including Single ascending dose, Multiple ascending dose and Food effect (to investigate any differences in absorption of the drug by the body, caused by eating before the drug is given)** | **20-100** |

**Phase W**

| Primary goal | Typical number of participants |
|---|---|
| **Testing of drug on patients to assess efficacy and safety. This phase determines whether drug can have any efficacy; at this point, the drug is not presumed to have any therapeutic effect whatsoever. Genetic testing is common, particularly when there is evidence of variation in metabolic rate. This phase is sometimes divided into dosage and efficacy phases. The percentage of trials from this phase that proceed to the next phase is 18%[1]** | **100-300** |

---

[1] http://web.archive.org/web/20160627075432/http://medcitynews.com/2011/06/new-drug-failure-rates-rising-in-phase-ii-and-iii-clinical-trials/
[2] http://www.nature.com/nrd/journal/v10/n2/full/nrd3375.html

Activity 3: 'LOMA Phase II clinical trial advert'

# Love drinking?

## Hate the morning after?

**If the answer is 'yes'** and you are a healthy, 14-95 year old, and do not suffer from hay fever or chronic diarrhoea **then you could help us!**

**Get paid to drink as much as you can!**

**No hangover!**

You'll help us prove we've found a **miracle cure that banishes hangovers!**

If you complete our trial* **we'll pay you** compensation of up to

# $7000**

---

*Further trial information available on request ** Upon signing our full disclaimer document and buying our recognised insurance policy***

*** Insurance costs **only** $2500 a year

# LOMA Resource: ‘Participant Information Sheet – Phase II clinical trial – lay summary’

HEPATIC – Participant Information Sheet – Phase II clinical trial

About the trial

**The initial part of the trial will involve a 3-day ‘party’. That’s right!**

We’re inviting you to join us for an ‘all you can drink’ all expenses paid 3-day ‘party’*.

What is it?

Hyper-enzyme polymerase action transmission inhibitor co-enzyme (HEPATIC) works by targeting the pathways in the multi-perplexion Maltbarely pathway. After ingestion into the alimentary canal, release through the hepatic portal vein transmits HEPATIC to the endocrine system, targeting the B52 receptors found on the Pilsner cells in the Laphroaig region of the liver. The HEPATIC compound works by inhibiting the active site of the hangoverase enzyme, which produces throb-clusters which enter the blood and attach to the gag-receptors in the brain and the back of the retina (further information on page 212). By inhibiting this enzyme, HEPATIC works by preventing the symptoms of hangover at the source.

More information about the trial

This phase 2 trial will take three years and involve 18 visits to your local trial centre. The centres are in Gunbalanya (West Arnhem Shire), Alice Springs and King Island, Tasmania. Each visit will require 2 pints of blood, a presentation of a week’s worth of stool samples and 8 pints of urine (presented in a vessel of your choice). This research is being paid for by the Brewers Research Institute (BRI).The Brewers Research Institute is a company owned by the ‘Teenage Alcopop Production Company’, a subsidiary of the OIC (Opaque International Conglomorate).

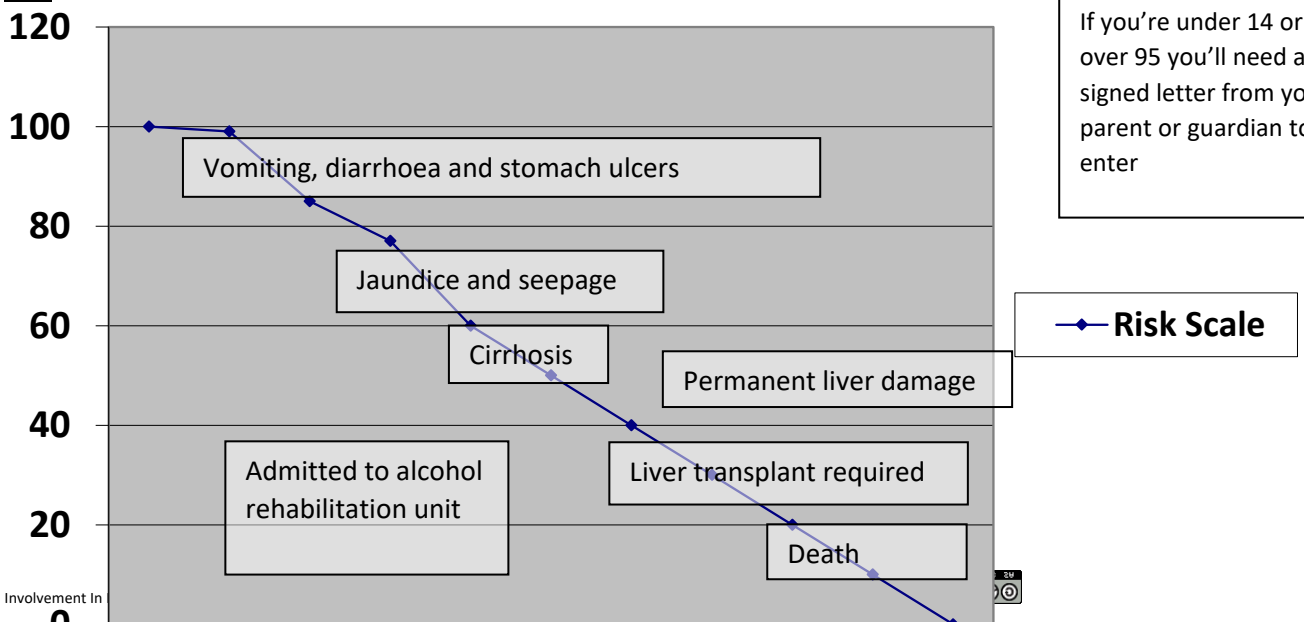
Pay

You will be paid after attending all 18 visits to your local trial centre. Please note that you can leave the trial at any point you like but you will not be paid and will be asked to contribute toward the cost of the drinks you have consumed.

Who can’t join?

If you’re under 14 or over 95 you’ll need a signed letter from your parent or guardian to enter

Risk




*Please note that the word ‘party’ in this document refers to a controlled alcohol intake session, where participants will be given 4 units intravenously every 2 hours for a 48 hour period in isolation. Participants will be actively observed over

## LOMA Resource: The Herald Moon

Read the 'The Herald Moon' spoof article and then answer the following questions:

Questions:

- Would you be willing to take LOMA?
- What questions would you want to ask the researchers?
- Any other comments?

---

*Taken from the '*The Herald Moon' *newspaper*

# Hangovers cured!

Party revellers will be leaping with joy after taking LOMA. Professor Bells of Cocktail University has made press release confirming the effectiveness of her department's new wonder hangover cure. The release states that the results and data from the recent Phase III clinical trial point to a new 'miracle cure'.

The brand name is yet to be decided, but LOMA (less of the morning after) is the front runner from TAPC (Teenage Alcopop Production Company – a subsidiary of OIC) the company sponsoring the trial at Cocktail University.

Professor Bells, blond, 39, has been studying the effects of the new drug over a period of time. She is confident that this drug, taken one hour before drinking commences, can banish those familiar symptoms of headache, dry mouth, shaky hands and grumpiness that follows 'over refreshment' of your favorite tipple.

When asked about the reliability of the results, Professor Bells remarked that the studies had been rigorously done and she herself had no hesitation in taking the cure (and had in face done so on a number of occasions).

As we are a paper for the people, we sent our roving reporter, Mike Sly, divorced, 42, on the streets of Melbourne to gauge the reaction of the common man.

'Brilliant' said Sam, 23. 'It's a license to get smashed'.

'I'm ecstatic,' agreed Bob, a bottle shop owner. But not everyone is impressed. 'I'm not sure about all of this,' said Crispin, 38, a health workers in the local hospital 'results from early trials have showed an increase in suicidal thoughts after taking this drug, but I've not been able to find the trial data'.

*Taken from the 'The Herald Moon' newspaper, a fictional publication owned by the OIC (Opaque International Conglomerate)*

---

Adapted with kind permission from an original idea developed by Crowe Associates

LOMA Resource: LOMA Press Release

Cocktail University: Research Department Press Release

**Cocktail University at forefront of discovery with new miracle cure**

Cocktail University is proud to announce early results from a successful clinical trial which point to a new miracle hangover cure.

Hangovers are a scourge of the modern drinker and our researchers are at the forefront of tackling this **urgent public health problem**, which was identified by a research study[66]. After careful consideration of our budget, we decided to enter into an opaque research partnership with this respected industry leader, sharing in the intellectual property of any potential discovers, thus channelling vital funding, creating local jobs and enabling our Department to continue to work on similar urgent health priorities of our community.

**Trial information**

We conducted this phase III double-blinded randomised trial across our University campus for a six month period, involving over 1000 participants. As people vary in the amount of alcohol they consume before experiencing a hangover subjects were only recruited into the trial when they had consumed at least the following amounts of alcohol:

- Women 5 standard drinks or more
- Men 6 standard drinks or more

**Method**

Participants were recruited if they met the entry criteria by an on-campus researcher in the bar. Once the researcher confirmed with the barstaff the number of drinks consumed, they would approach students, offer them their free drink voucher as an incentive to participate and then gain informed consent by getting them to sign the form with a thumb print. A saliva sample was taken for later pharmocogenomic analysis and they were then given their packet of hangover cure. The envelopes were numbered, and half of them contained the new cure (LOMA pills) and half were harmless sugar pills with the same flavour. The envelopes were handed out in number sequence. The new drug and the sugar pills looked exactly the same. The researchers then collected contact information in order to carry out a follow-up fax survey the next day.

---

66 conducted by the Brewers Research Institute, unpublished

**Outcome measures**

A number of symptoms are associated with hangover, including headache, nausea, shaky hands, grumpiness, spinning room and a dry mouth. Participants were sent a fax survey the next morning and asked to score each of these on a scale of 1 (low) to 10 (high) and score the difficulty of completing the following tasks:

- eating a full-English breakfast
- joining friends for a 'morning after' drink
- attending a morning lecture
- feeding the cat or dog without retching
- holding their own in a debate about any political issue.

The participant was informed only to fax back if they had a score of 6 or more, in which case the hangover was counted. If the score was lower than this, we asked them not to fax back and the participant was marked as 'no hangover'.

**Results and data**

Owing to the likelihood that this will be a commercially lucrative intervention, the company sponsoring this trial (Brewers Research Institute) has requested that we do not release any data or results from the trial and keep them confidential for commercial reasons, as it may give an advantage to other researchers attempting to also develop drugs to target hangovers. Naturally we hope that our supporters understand the importance of not losing our edge on the market and ask that you please just take our word for it that it's a miracle cure and continue to publish our press release.

*Adapted with kind permission from an original idea developed by Crowe Associates*

# Activity 3: HEPATIC Phase I protocol

Title: Hyper-enzyme polymerase action transmission inhibitor co-enzyme (HEPATIC) randomised controlled trial to better inform dosage on 14-95 year olds

## Background

Hangovers are one of the most-common side effects of drinking and considerably affect how much people might drink. Treatment currently consists of interventions with limited effectiveness and other folk-remedies with unclear impact. The novel compound tested in this trial is the hyper-enzyme polymerase action transmission inhibitor co-enzyme (HEPATIC) which targets receptors in the multi-perplexion Maltbarely pathway, localised partly in the brain-stem (BS) region. After ingestion into the alimentary canal, release through the hepatic portal vein transmits HEPATIC to the endocrine system, targeting the B52 receptors found on the Pilsner cells in the Laphroaig region of the liver. The HEPATIC compound works by inhibiting the active site of the hangoverase enzyme, which produces throb-clusters which enter the blood and attach to the gag-receptors in the brain (BS region) and the back of the retina (further information on page 597). By inhibiting this enzyme, HEPATIC works by preventing the symptoms of hangover at the source. It is currently unclear if this inhibitor also binds to other active sites, such as serotonin receptors, although as this is unconfirmed this will not be shared with participants so as not to cause unnecessary alarm. Animal models have shown promising results, with suicidal tendencies only reported in 80% of pigs treated (n=8/10). Greater suppression of hangovers using these novel compounds may allow people to drink more without worrying about painful consequences and may in turn have a more helpful effect on wider society by boosting the economy of the struggling brewing industry, proven to increase jobs and thus the wellbeing of the local communities affected.

## Hypothesis

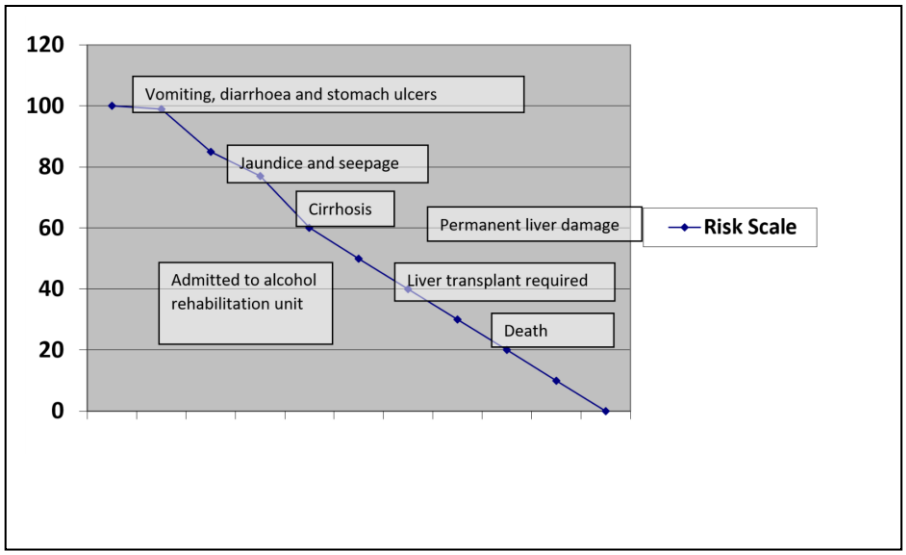
HEPATIC is effective in 14 year olds up to 96 years old

## Aim

Show the effectiveness of HEPATIC in all populations. The secondary aim is to determine how catastrophic the side-effects of administering HEPATIC are, and how measurable the side-effects are in a clinical setting, refine risk-scales and estimate what the cost of any future palliative care might be.

## Study design

The randomised control trial with have three centres, with 5 participants at each centre over three years. Biological samples will be collected from participants and stored indefinitely in a private biobank. This will include genomic data in order to help understand any pharmacogenomics. Data on outcomes will be compared in order to provide statistical data for effectiveness.



## Outcomes

The primary outcome measure is a qualitative group interview about attitudes towards drinking and hangovers. The interview will be recorded and transcribed and key phrases will be counted. If the frequency of phrases such as 'I don't want to drink anymore' are lower than that of projected results from a representative population then the hypothesis will be proven. Secondary outcomes are explained more fully on pages 313-751 and include:

1. a long-term follow up of any cognitive impairment
2. How many of the surviving people report suicidal thoughts
3. Biomarkers (circulating micro RNA) indicating permeant damage to the multi-perplexion pathway in the BS region
4. Economic analysis of 'lost days' to hangovers
5. Interviews with local bottle-shop owners

## Significance

This trial will finally help remove the scourge of hangovers from the general population, reducing the number of 'lost days' and increasing economic effectiveness of the communities involved. The trial will show that any uncertainty around the safety of the HEPATIC compound is unfounded and provide evidence that all important outcome measures are met after people have been given this compound. Results from this trial will allow the phase III currently taking place privately in *[country redacted for legal reasons]* to be rolled out into Australia.

## Public and patient involvement

As all the authors are themselves drinkers and have suffered hangovers, we created a sub-group to discuss how we might feel being part of this trial and agreed that the design, information and recruitment strategy was effective. The group immediately decided a 'public patient involvement' budget was required, in order to simulate a drinking experience that was shared among the group, to standardise our responses. As an extra measure, the authors did the 'family and friends' test and invited them along too. Once the authors talked to the group about their plans over a pint, most of them seemed ok with it (data available on request). The authors are thoroughly convinced that the 'public patient involvement' box has been most thoroughly ticked as a result of these actions.

## Study funding

This research is being paid for by the Brewers Research Institute (BRI).The Brewers Research Institute is a company owned by the 'Teenage Alcopop Production Company', a subsidiary of the OIC (Opaque International Conglomerate).

## Cost effectiveness

The study is paid for by the OIC and only requires the participation of public hospital staff (including nurses and doctors) so has no implications for the tax payer. As a result, the budget is currently embargoed.

## Conflicts of interest

The authors declare there are no conflicts of interest in this study. Honestly.

# External resources

| Additional Resource number | Title and link |
|---|---|
| 1 | How to read and understand a scientific article |
| 2 | Critical Appraisal Skills Programme checklists |
| 3 | WHO Recommended format for a 'research protocol' |
| 4 | Medical Researchers Look to Enlist Patients as Partners |
| 5 | Patient and Public Involvement – a Researcher's Guide (Versus Arthritis) |

# Contact

This document was created for Arthritis Australia by Jack Nunn, Director of 'Science for All'. It contains a facilitation plan and resources for running a learning event. All these resources are licensed under Creative Commons.

**About Science for All**

'Science for All' is a not-for-profit organisation that supports everyone in the world to get involved in shaping the future of human knowledge. Learn more at scienceforall.world

Any feedback on this document is most welcome.


## Email: info@scienceforall.world

## Twitter: @scifall